Baskar
10/030740

FILE 'REGISTRY' ENTERED AT 12:03:11 ON 08 OCT 2003
E HEMAGGLUTIN/CN
L1 2089 S HEMAGGLUTININ?/CN
E FHAB/CN 5

- key terms

FILE 'HCAPLUS' ENTERED AT 12:03:30 ON 08 OCT 2003
L1 2089 SEA FILE=REGISTRY ABB=ON PLU=ON HEMAGGLUTININ?/CN
L2 1068 SEA FILE=HCAPLUS ABB=ON PLU=ON (FILAMENT?(W)(HEMAGGLUTI N? OR HAEMAGLUTIN?) OR FHA) OR L1 OR FHAB
L4 22 SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND (MENINGIT? OR MENINGOCOC?)
L5 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 AND (ORF OR OPEN(1W)F RAME OR VACCIN? OR IMMUNIS? OR IMMUNIZ? OR IMMUNOGEN?)

L5 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:300440 HCAPLUS
DOCUMENT NUMBER: 138:319681
TITLE: Genetically-detoxified pertussis holotoxin as proteinaceous adjuvant
INVENTOR(S): Gajewczyk, Diane M.; Boux, Heather A.; Novak, Anton; Klein, Michel H.
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 25 pp., Cont.-in-part of U.S. Ser. No. 258,228.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003072774	A1	20030417	US 1995-481878	19950607
CA 2192454	AA	19951221	CA 1995-2192454	19950608
EP 1149588	A1	20011031	EP 2001-201598	19950608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1149589	A1	20011031	EP 2001-201610	19950608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
ES 2179105	T3	20030116	ES 1995-924122	19950608

PRIORITY APPLN. INFO.: US 1994-258228 A2 19940610
EP 1995-924122 A3 19950608

AB A modulated immune response to an antigen is achieved by coadministering the antigen and a genetically-detoxified pertussis holotoxin, particularly one retaining its **immunogenicity**, to a host. The modulated immune response enables **immunogenic** compns., including multivalent pediatric **vaccines**, such as DTP, to be provided which produce a modulated immune response in the absence of extrinsic adjuvants, such as alum. The adjuvanting effect achieved by the genetically-detoxified pertussis holotoxin enables at least the same level of a modulated immune response to a non-Bordetella antigen to be achieved as previously attained by alum, without the undesirable side effects thereof. Modifications are possible within the scope of the disclosed invention.

L5 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:793458 HCAPLUS
DOCUMENT NUMBER: 137:293549
TITLE: Multi-valent **vaccine** compositions
INVENTOR(S): Boutriau, Dominique; Capiau, Carine; Desmons, Pierre Michel; Lemoine, Dominique; Poolman, Jan
PATENT ASSIGNEE(S): Glaxosmithkline Biologicals S.A., Belg.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080965	A2	20021017	WO 2002-EP3573	20020328

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-8364 A 20010403

AB The present invention relates to new, advantageous DTP-based combination **vaccine** formulations, and concomitantly administered combination **vaccine** kits. Methods of administration of these **vaccines** and kits are also provided. The multi-valent composition can protect against Bordetella pertussis, Clostridium tetani, Corynebacterium diphtheriae, hepatitis B virus, polio virus, Streptococcus pneumoniae, Neisseria **meningitidis**, and Haemophilus influenzae. The multi-valent composition comprises pertussis toxin, **filamentous hemagglutinin**, diphtheria toxin, HBsAg, inactivated polio virus, and various capsular polysaccharides conjugated to carrier proteins.

L5 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:754696 HCAPLUS
DOCUMENT NUMBER: 137:293520
TITLE: Antibody-containing sera for identifying Pathogenic and commensal bacteria antigens as **vaccines**
INVENTOR(S): Robinson, Andrew; Gorringe, Andrew Richard; Hudson, Michael John; Bracegirdle, Philippa; West, David McKay; Oliver, Kerry Jane; Kroll, John Simon; Langford, Paul Richard
PATENT ASSIGNEE(S): Microbiological Research Authority, UK; Imperial College Innovations Limited
SOURCE: PCT Int. Appl., 310 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002077648	A2	20021003	WO 2002-GB1399	20020322

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-7219 A 20010322

AB The invention provides methods of screening commensal and pathogenic bacteria for previously unidentified **vaccine** antigens, based upon identifying polypeptide antigens that bind to sera raised against commensal bacterial proteins. Also provided are **vaccine** compns. and methods of preparing **vaccine** compns. comprising the antigens identified by the screening methods. Antigens and uses thereof are also described.

IT **467261-09-2 467261-10-5**
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; antibody-containing sera for identifying Pathogenic and commensal bacteria antigens as **vaccines**)

L5 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:521541 HCAPLUS
DOCUMENT NUMBER: 137:77880
TITLE: Ribosomal complexes with microbial polynucleotides for mucosal **vaccination**
INVENTOR(S): Timmerman, Benedikt
PATENT ASSIGNEE(S): Fr.
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053189	A2	20020711	WO 2002-IB738	20020104

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

SN, TD, TG

GB 2370839 A1 20020710 GB 2001-758 20010106

PRIORITY APPLN. INFO.: GB 2001-758 A 20010106

AB The author discloses **immunogenic** complexes comprising a ribosomal particle complex of a microbe and a polynucleotide mol. encoding an antigen. The ribosomal particle complex is composed of the subunits of ribosomes (50 S and 30 S subunits in bacteria and 60 S and 40 S subunits in eukaryotes), with the ribosomal subunits generally retaining sufficient integrity to preserve the double-stranded nature of the large r-RNA's (16 S and 23S in bacteria; 18S and 28S in eukaryotic cytosol) contained in the ribosomal subunits. In one example, Bordetella pertussis ribosomal complexes were first derivatized with maleimide and conjugated to a thiol-derivatized cDNA encoding **filamentous hemagglutinin**. Nasal **immunization** of mice demonstrated a protective response.

L5 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:642797 HCAPLUS

DOCUMENT NUMBER: 135:317114

TITLE: Production of Neisseria **meningitidis** transferrin-binding protein B by recombinant Bordetella pertussis

AUTHOR(S): Coppens, Isabelle; Alonso, Sylvie; Antoine, Rudy; Jacob-Dubuisson, Francoise; Renauld-Mongenie, Genevieve; Jacobs, Eric; Locht, Camille

CORPORATE SOURCE: Laboratoire de Microbiologie Genetique et Moleculaire, INSERM U447, Institut Pasteur de Lille, Lille, F-59019, Fr.

SOURCE: Infection and Immunity (2001), 69(9), 5440-5446 CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Neisseria **meningitidis** serogroup B infections are among the major causes of fulminant septicemia and **meningitis**, especially severe in young children, and no broad **vaccine** is available yet. Because of poor **immunogenicity** of the serogroup B capsule, many efforts are now devoted to the identification of protective protein antigens. Among those are PorA and, more recently, transferrin-binding protein B (TbpB). In this study, TbpB of N. **meningitidis** was genetically fused to the N-terminal domain of the Bordetella pertussis **filamentous hemagglutinin** (**FHA**), and the **fha**-tbpB hybrid gene was expressed in B. pertussis either as a plasmid-borne gene or as a single copy inserted into the chromosome. The hybrid protein was efficiently secreted by the recombinant strains, despite its large size, and was recognized by both anti-**FHA** and anti-TbpB antibodies. A single intranasal administration of recombinant virulent or pertussis-toxin-deficient, attenuated B. pertussis to mice resulted in the production of antigen-specific systemic IgG, as well as local IgG and IgA. The anti-TbpB serum antibodies were of the IgG1, IgG2a, and IgG2b isotypes and were found to express complement-mediated bactericidal activity against N. **meningitidis**. These observations indicate that recombinant B. pertussis may be a promising vector for the development of a mucosal **vaccine**

against serogroup B **meningococci.**
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:101328 HCAPLUS
DOCUMENT NUMBER: 134:146387
TITLE: Immuno-protective and non-toxic Gram-neg. bleb **vaccine** suitable for pediatric use
INVENTOR(S): Berthet, Francois-xavier Jacques; Dalemans, Wilfried L. J.; Denoel, Philippe; Dequesne, Guy; Feron, Christiane; Lobet, Yves; Poolman, Jan; Thiry, Georges; Thonnard, Joelle; Voet, Pierre
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S.A., Belg.
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009350	A2	20010208	WO 2000-EP7424	20000731
WO 2001009350	A3	20010830		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000012974	A	20020507	BR 2000-12974	20000731
EP 1208214	A2	20020529	EP 2000-956369	20000731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506049	T2	20030218	JP 2001-514142	20000731
EP 1307224	A2	20030507	EP 2001-965152	20010731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002000506	A	20020402	NO 2002-506	20020131

PRIORITY APPLN. INFO.:
GB 1999-18319 A 19990803
WO 2000-EP7424 W 20000731
GB 2001-3170 A 20010208
WO 2001-EP8857 W 20010731

AB The present invention relates to an immuno-protective and non-toxic Gram-neg. bleb **vaccine** suitable for pediatric use. Examples of the Gram-neg. strains from which the blebs are made are N. **meningitidis**, M. catarrhalis and H. influenzae. The blebs of the invention are improved by one or more genetic changes to the chromosome of the bacterium, including up-regulation of protective antigens, down-regulation of immunodominant non-protective antigens, and detoxification of the Lipid A moiety of LPS.

L5 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:50126 HCAPLUS
DOCUMENT NUMBER: 134:130251
TITLE: Neisseria **meningitidis** compounds and anti-infection applications thereof
INVENTOR(S): Nassif, Xavier; Tinsley, Colin
PATENT ASSIGNEE(S): Institut National De La Sante Et De La Recherche Medicale (Inserm), Fr.; Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften E.V.
SOURCE: Eur. Pat. Appl., 237 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1069133	A1	20010117	EP 1999-401764	19990713
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2001004150	A2	20010118	WO 2000-EP6943	20000705
WO 2001004150	A3	20011213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1194446	A2	20020410	EP 2000-956222	20000705
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: EP 1999-401764 A 19990713
WO 2000-EP6943 W 20000705

AB The invention provides novel Neisseria **meningitidis** (Nm) polypeptides and polynucleotides which cover the Nm genetic diversity, and which correspond to polypeptide of Nm outer membrane and/or periplasma, and to methods for producing such Nm compds. Also provided are anti-Nm infection, and particularly diagnostic, prophylactic and therapeutic uses thereof.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:12649 HCAPLUS
DOCUMENT NUMBER: 134:99566
TITLE: **Vaccine** delivery system using Vibrio cholerae bacteria expressing heterologous antigens
INVENTOR(S): Pizza, Mariagrazia
PATENT ASSIGNEE(S): Chiron S.P.A., Italy
SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000857	A1	20010104	WO 2000-IB974	20000623
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1194576	A1	20020410	EP 2000-942323	20000623
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003503066	T2	20030128	JP 2001-506849	20000623

PRIORITY APPLN. INFO.: GB 1999-14960 A 19990625
WO 2000-IB974 W 20000623

AB The invention relates to delivery systems for heterologous antigens. Chromosomal loci within rRNA operons such as those of the 16S or the 23S genes have been identified as useful sites for the integration of nucleic acids into the chromosome of Vibrio cholerae bacteria. A particularly useful regulatory sequence for the direction of high level expression of heterologous antigens in this bacterium has been identified as the OmpU promoter.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:112849 HCAPLUS
DOCUMENT NUMBER: 133:133858
TITLE: A nasal whole-cell pertussis **vaccine** induces specific systemic and cross-reactive mucosal antibody responses in human volunteers
AUTHOR(S): Berstad, A. K. H.; Holst, J.; Froholm, L. O.; Haugen, I. L.; Wedege, E.; Oftung, F.; Haneberg, B.
CORPORATE SOURCE: Departments of Vaccinology, National Institute of Public Health, Oslo, N-0403, Norway
SOURCE: Journal of Medical Microbiology (2000), 49(2), 157-163
CODEN: JMMIAV; ISSN: 0022-2615
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A whole-cell pertussis **vaccine**, each dose consisting of 250 μg of protein, was given intranasally four times at weekly intervals to six adult volunteers. All **vaccinees** responded with increases in nasal fluid IgA antibodies to Bordetella pertussis whole-cell antigen. Three **vaccinees** with high nasal antibody responses also developed increased serum IgA and IgG antibodies to this antigen. Salivary antibody responses to the whole-cell antigen, as well as antibodies in serum and secretions to pertussis toxin (PT) and **filamentous hemagglutinin** (**FHA**) were negligible, except for a moderate increase in nasal fluid antibodies to **FHA**. Unexpectedly, the same **vaccinees** developed significant rises in nasal and salivary

IgA antibodies to **meningococcal** outer-membrane antigens, whereas corresponding serum IgA and IgG antibodies were unchanged. Thus it appears that mucosal **immunization** may induce secretory antibodies with broader specificities than can be found in serum.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:597423 HCAPLUS
DOCUMENT NUMBER: 131:213104
TITLE: Antigenic conjugates of conserved lipopolysaccharides of gram negative bacteria
INVENTOR(S): Arumugham, Rasappa G.; Fortuna-Nevin, Maria; Apicella, Michael A.; Gibson, Bradford W.
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 941738	A1	19990915	EP 1999-301747	19990309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9919540	A1	19990923	AU 1999-19540	19990309
JP 11322793	A2	19991124	JP 1999-61354	19990309
BR 9902008	A	20000509	BR 1999-2008	19990309

PRIORITY APPLN. INFO.: US 1998-37529 A 19980310

AB Antigenic conjugates are provided which comprise a carrier protein covalently bonded to the conserved portion of a lipopolysaccharide of a gram neg. bacteria, wherein said conserved portion of the lipopolysaccharide comprises the inner core and lipid A portions of said lipopolysaccharide, said conjugate eliciting a cross reactive immune response against heterologous strains of said gram neg. bacteria. The carrier protein is selected from CRM197, tetanus toxin, diphtheria toxin, pseudomonas exotoxin A, cholera toxin, group A streptococcal toxin, pneumolysin of Streptococcus pneumoniae, **filamentous hemagglutinin** (**FHA**), **FHA** of Bordetella pertussis, pili or pilins of Neisseria gonorrhoeae or **meningitidis**, outer membrane proteins of Neisseria **meningitidis**, C5A peptidase of Streptococcus and surface protein of Moraxella catarrhalis.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:483302 HCAPLUS
DOCUMENT NUMBER: 131:125480
TITLE: Bordetella pertussis **filamentous hemagglutinin**-based peptides which inhibit adhesion between leukocytes and endothelial cells

INVENTOR(S): Tuomanen, Elaine; Masure, H. Robert
PATENT ASSIGNEE(S): The Rockefeller University, USA
SOURCE: U.S., 82 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5932217	A	19990803	US 1994-348353	19941130
EP 584273	A1	19940302	EP 1992-913635	19920504
EP 584273	B1	19981230		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06507641	T2	19940901	JP 1992-512001	19920504
AU 664849	B2	19951207	AU 1992-21687	19920504
AU 9221687	A1	19921221		
AT 175122	E	19990115	AT 1992-913635	19920504
US 5792457	A	19980811	US 1995-465929	19950606
US 5968512	A	19991019	US 1995-465965	19950606
US 6015560	A	20000118	US 1995-465966	19950606

PRIORITY APPLN. INFO.: US 1994-247572 B2 19940523
US 1991-695613 A 19910503
WO 1992-US3725 W 19920504
US 1994-348353 A3 19941130

AB Peptides which will inhibit the reaction between the RGD tripeptide of Bordetella pertussis **filamentous hemagglutinin** (**FHA**) and the integrin receptors of endothelial cells and their utility as therapeutic agents are described. **FHA** is discovered to comprise polypeptide regions with binding properties homologous to those of C3bi, blood-coagulation factor X, and an integrin receptor on endothelial cells. They are also antigenically related and antibodies to **FHA** cross-react with endothelial cells. Peptide regions of **FHA** can bind to leukocytes and competitively inhibit binding of Factor X or C3bi to leukocytes or leukocytes to endothelial cells. Significant consequences of these discoveries are: (1) peptides which contain or are analogs of the RGD region or one of the Factor X regions of **FHA** will bind to the CR3 integrin of leukocytes, thereby preventing adherence of the leukocyte to endothelial cells in a procedure for lessening deleterious inflammation; (2) peptides or analogs which interact with leukocytes in competition with Factor X or C3bi can be used to inhibit blood coagulation or opsonization and phagocytosis; (3) antibodies to **FHA** will bind to homologous regions of normal proteins in animals; (4) peptides containing the carbohydrate recognition domain or analogs are optimal **vaccines** for whooping cough; and (5) peptides of each of the endothelial cell integrin receptor, Factor X, or C3bi domains of **FHA** are useful in **vaccine** quality control.

IT **233752-12-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; Bordetella pertussis **filamentous hemagglutinin**-based peptides which inhibit adhesion between leukocytes and endothelial cells)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE

FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L5 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:204276 HCAPLUS
DOCUMENT NUMBER: 129:1147
TITLE: Cloning and characterization of the genomic RNA sequence of the mumps virus strain associated with a high incidence of aseptic **meningitis**
AUTHOR(S): Saito, Hiroyuki; Takahashi, Yoshihiro; Harata, Seizaburo; Tanaka, Keiko; Sato, Hiroyasu; Suto, Tsunehisa; Yamada, Akio; Yamazaki, Shudo; Morita, Morihiro
CORPORATE SOURCE: Dep. Microbiology, Akita Prefectural Inst. Public Health, Akita, 010-0874, Japan
SOURCE: Microbiology and Immunology (1998), 42(2), 133-137
CODEN: MIIMDV; ISSN: 0385-5600
PUBLISHER: Center for Academic Publications Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CDNA clones of the mumps virus wild-type strain, associated with a high incidence of aseptic **meningitis** (ODATE-1 strain), were isolated and analyzed from genomic nucleotide position 22 to 8520 containing the NP, P, M, F, SH and HN protein coding region. The ODATE-1 strain exhibited a RFLP profile identical to that of the Urabe **vaccine** strain in spite of the fact that the virus was isolated from non-**vaccinated** cases. However,a comparison of nucleotide and amino acid sequences among the ODATE-1 strain, Urabe strain and Miyahara strain revealed that the ODATE-1 strain was not related to the Urabe strain.
IT **207354-78-7**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; cloning, characterization and sequence of the genomic RNA sequence of the mumps virus strain associated with a high incidence of aseptic **meningitis**)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:71413 HCAPLUS
DOCUMENT NUMBER: 124:115448
TITLE: Genetically-detoxified pertussis holotoxin as adjuvants
INVENTOR(S): Gajewczyk, Diane M.; Boux, Heather A.; Novak, Anton; Klein, Michel H.
PATENT ASSIGNEE(S): Connaught Laboratories Ltd., Can.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9534323	A2	19951221	WO 1995-CA341	19950608
WO 9534323	A3	19960118		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2192454	AA	19951221	CA 1995-2192454	19950608
AU 9528765	A1	19960105	AU 1995-28765	19950608
EP 764029	A1	19970326	EP 1995-924122	19950608
EP 764029	B1	20020626		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
EP 1149588	A1	20011031	EP 2001-201598	19950608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1149589	A1	20011031	EP 2001-201610	19950608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 219686	E	20020715	AT 1995-924122	19950608
ES 2179105	T3	20030116	ES 1995-924122	19950608

PRIORITY APPLN. INFO.:	US 1994-258228	A	19940610
	EP 1995-924122	A3	19950608
	WO 1995-CA341	W	19950608

AB Compns. containing genetically-detoxified pertussis holotoxin and a non-Bordetella or Bordetella antigen are used as adjuvant for **vaccines**. The modulated immune response enables **immunogenic** compns., including multivalent pediatric **vaccines** such as DTP, to be provided which produce a modulated immune response in the absence of extrinsic adjuvants such as alum. The adjuvanting effect achieved by the genetically-detoxified pertussis holotoxin enables at least the same level of adjuvanting effect to be achieved as previously attained by alum, without the undesirable side effects thereof. Also, disclosed are **vaccines** containing the adjuvant composition and other antigen, such as cancer-associated antigen and pathogen.

L5 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	1996:2566 HCAPLUS
DOCUMENT NUMBER:	124:84240
TITLE:	Intranasal **immunization** of mice against influenza with synthetic peptides anchored to proteosomes
AUTHOR(S):	Levi, Raphael; Aboud-Pirak, Esther; Leclerc, Claud; Lowell, George H.; Arnon, Ruth
CORPORATE SOURCE:	Department Chemical Immunology, Weizmann Institute Science, Rehovot, 76100, Israel
SOURCE:	Vaccine (1995), 13(14), 1353-9 CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER:	Elsevier
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Synthetic **vaccines** that are based on peptides representing **immunogenic** epitopes require a carrier mol. as well as an adjuvant to be effective. The choice of carriers or adjuvants

approved for use in humans is very limited, and a considerable effort is devoted to develop new and efficient delivery systems. One of these vehicles utilizes prepns. of outer membranes of **meningococci**, that form hydrophobic interactions, denoted proteosomes. **Immunogenic** proteins and peptides can be anchored to these proteosomes vesicles, which may serve as both carrier and adjuvant functions. In the present study the authors examined the ability of proteosomes to present epitopes of influenza, to elicit specific anti-influenza responses and to protect mice against viral challenge after intranasal **immunization**. Three influenza peptides were used, one corresponding to amino acid residues 91-108 of the hemagglutinin surface glycoprotein of H3 subtype, which comprises a B-cell epitope, and two from the internal nucleoprotein--a T-helper cell (Th) epitope (residues 55-69) and a cytotoxic T-lymphocyte (CTL) epitope (147-158). Mice were **immunized** intranasally (i.n.) with prepns. containing each of the above epitopes, or various combinations thereof. The results obtained with this system demonstrate that influenza epitopes represented by synthetic peptides anchored to a proteosome carrier elicit both humoral and cellular specific immune responses, that can lead to partial protection of the mice from viral challenge. The importance of **immunizing** with **vaccines** containing both B- and T-cell peptide epitopes was emphasized by the demonstration that such **vaccines** elicited longer lasting immunity and led to more effective protection against influenza viral challenge.

IT **152343-71-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**vaccine** for influenza using B and T cell epitopes anchored to proteosomes)

L5 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:2261 HCAPLUS
DOCUMENT NUMBER: 120:2261
TITLE: Cloning and expression of high molecular weight surface proteins of non-typeable Haemophilus
INVENTOR(S): Barenkamp, Stephen J.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9319090	A1	19930930	WO 1993-US2166	19930316
W: AU, BR, CA, FI, JP, KR, NO, RU, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9339168	A1	19931021	AU 1993-39168	19930316
AU 669360	B2	19960606		
EP 632814	A1	19950111	EP 1993-908295	19930316
EP 632814	B1	20020828		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL,				

PT, SE				
JP 07506248	T2	19950713	JP 1993-516604	19930316
BR 9306109	A	19971118	BR 1993-6109	19930316
RU 2157816	C2	20001020	RU 1994-42726	19930316
CA 2131837	C	20020212	CA 1993-2131837	19930316
AT 222955	E	20020915	AT 1993-908295	19930316
ES 2183812	T3	20030401	ES 1993-908295	19930316
NO 9403431	A	19941110	NO 1994-3431	19940915
FI 9404273	A	19941115	FI 1994-4273	19940915
US 5603938	A	19970218	US 1994-302832	19941005
US 5876733	A	19990302	US 1995-469880	19950606
US 5977336	A	19991102	US 1996-617697	19960401
US 6218141	B1	20010417	US 1996-719641	19960925
PRIORITY APPLN. INFO.:			GB 1992-5704 A	19920316
			WO 1993-US2166 A	19930316
			US 1994-302832 A1	19941005

AB The genes for high mol. weight surface proteins HMW1 and 2 of H. influenzae are cloned and sequenced. The amino acid sequences of HMW1 and 2 derived from the genes had high homol. with that of the **filamentous hemagglutinin** of Bordetella pertussia. The HMW1 and 2 are useful for preparation of protective antigens against nontypeable Haemophilus-associated diseases such as otitis, sinusitis, bronchitis, etc., and as carrier for the protective Hib carrier polysaccharides in a conjugate **vaccine** against **meningitis**. The genes for the high mol. weight surface proteins were cloned from a genomic library of H. influenzae constructed on λEMBL3 by immunol. screening using an human antibody against the high mol. weight surface proteins. Also shown was the adherence of the HMW1 and 2 on the Chang epithelial cells. HMW3 and 4 were also cloned and partially sequenced.

L5 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:181163 HCAPLUS
DOCUMENT NUMBER: 116:181163
TITLE: **Filamentous hemagglutinin** of Bordetella pertussis as a carrier molecule for conjugate **vaccines**
INVENTOR(S): Kimura, Alan; Dick, William Edwin, Jr.; Cowell, James Leo
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 471177	A2	19920219	EP 1991-110919	19910702
EP 471177	A3	19930224		
EP 471177	B1	19951004		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE				
AT 128628	E	19951015	AT 1991-110919	19910702
JP 04230634	A2	19920819	JP 1991-222392	19910808
CA 2048917	AA	19920214	CA 1991-2048917	19910809
NO 9103130	A	19920214	NO 1991-3130	19910812
FI 9103820	A	19920214	FI 1991-3820	19910812

AU 9181789 A1 19920220 AU 1991-81789 19910812
AU 649700 B2 19940602
PRIORITY APPLN. INFO.: US 1990-565161 19900813
AB A **vaccine** contains an **immunogenic** conjugates comprising an antigen bound to a **filamentous hemagglutinin** (**FHA**) of B. pertussis. Purified **FHA** from B. pertussis was mixed with polyribosylribitol phosphate (I) from Haemophilus influenzae type b and lyophilized, then it was redispersed in DMSO before addition of Na cyanoborohydride to initiate reductive amination to thereby conjugate the **FHA** and I. NaBH4 was added to the mixture to cap the reaction and then lyophilized, washed, purified, and again lyophilized. The I-**FHA** conjugate was adsorbed to Al3(PO4) adjuvant and 2 s.c. injections of 35μg protein were given to mice at 4 wk intervals. Mice at 3 and 4 wk post-**immunization** had 2.3, and 5.18 μg/mL of anti-I antibody and after the 2nd **immunization** at wk 4, the anti-I antibody responses was boosted to 26.53 μg/mL 6 wk postimmunization. Anti-**FHA** antibody was also high as compared to controls.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 12:16:00 ON 08 OCT 2003)
L6 49 S L5
L7 29 DUP REM L6 (20 DUPLICATES REMOVED)

L7 ANSWER 1 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-625512 [59] WPIDS
CROSS REFERENCE: 1996-049422 [05]
DOC. NO. CPI: C2003-170883
TITLE: New pertussis **vaccines** comprising a genetically-detoxified pertussis holotoxin and another, non-Bordetella antigen, useful as a **vaccine**, or adjuvant to increase the immune response, against e.g. whooping cough or cancer.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): BOUX, H A; GAJEWCZYK, D M; KLEIN, M H; NOVAK, A
PATENT ASSIGNEE(S): (BOUX-I) BOUX H A; (GAJE-I) GAJEWCZYK D M; (KLEI-I) KLEIN M H; (NOVA-I) NOVAK A
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003072774	A1	20030417	(200359)*		25

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003072774	A1 CIP of	US 1994-258228	19940610
		US 1995-481878	19950607

PRIORITY APPLN. INFO: US 1995-481878 19950607; US 1994-258228 19940610
AN 2003-625512 [59] WPIDS
CR 1996-049422 [05]
AB US2003072774 A UPAB: 20030915

NOVELTY - An **immunogenic** composition comprising a genetically-detoxified pertussis holotoxin, which is present in an amount sufficient to modulate an immune response to the other antigen in the absence of an extrinsic adjuvant, and at least one other, non-Bordetella, antigen, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for obtaining a modulated immune response to an antigen in a host, comprising:

(a) administering the non-Bordetella antigen to the host; and

(b) co-administering to the host the genetically-detoxified holotoxin.

ACTIVITY - Antibacterial; Cytostatic.

B16 mouse melanoma model was used to assess the effectiveness of genetically-detoxified pertussis holotoxin (K9G129) as an adjuvant in cancer immunotherapy. Mice were **immunized** with the new composition, and challenged with 105 live B16 melanoma cells. Results showed that even the lowest concentration of K9G129 was effective in causing a delay in tumor appearance. The results indicate that K9G129 can act as an adjuvant in cancer immunotherapy to increase the immune response towards tumor cells.

MECHANISM OF ACTION - **Vaccine**.

USE - The composition or method is useful for obtaining a modulated immune response to an antigen in a host, e.g. a human (claimed). The composition is particularly useful as a **vaccine** against pertussis or whooping cough. The composition may also be used as a **vaccine** against diphtheria, tetanus or cancer. The composition is also useful as an adjuvant in immunotherapy to increase the immune response to an antigen.

Dwg.0/9

L7 ANSWER 2 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER:	2003194353 EMBASE
TITLE:	**Vaccine** adjuvants.
AUTHOR:	Glenn G.
CORPORATE SOURCE:	Dr. G. Glenn, IOMAI Corporation, 20 Firstfield Road, Gaithersburg, MD 20878, United States. gglenn@iomai.com
SOURCE:	Expert Review of Vaccines, (2003) 2/2 (163-164). Refs: 7 ISSN: 1476-0584 CODEN: ERVXAX
COUNTRY:	United Kingdom
DOCUMENT TYPE:	Journal; Editorial
FILE SEGMENT:	026 Immunology, Serology and Transplantation 037 Drug Literature Index 039 Pharmacy
LANGUAGE:	English

L7 ANSWER 3 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER:	2003018876 EMBASE
TITLE:	Distribution and function of new bacterial intein-like protein domains.
AUTHOR:	Amitai G.; Belenkiy O.; Dassa B.; Shainskaya A.; Pietrokovski S.
CORPORATE SOURCE:	S. Pietrokovski, Molecular Genetics Department, Weizmann Institute of Science, Rehovot 76100, Israel. pietro@bioinfo.weizmann.ac.il

SOURCE: Molecular Microbiology, (2003) 47/1 (61-73).
Refs: 31
ISSN: 0950-382X CODEN: MOMIEE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Hint protein domains appear in inteins and in the C-terminal region of Hedgehog and Hedgehog-like animal developmental proteins. Intein Hint domains are responsible and sufficient for protein-splicing of their host-protein flanks. In Hedgehog proteins the Hint domain autocatalyses its cleavage from the N-terminal domain of the Hedgehog protein by attaching a cholesterol molecule to it. We identified two new types of Hint domains. Both types have active site sequence features of Hint domains but also possess distinguishing sequence features. The new domains appear in more than 50 different proteins from diverse bacteria, including pathogenic species of humans and plants, such as Neisseria **meningitidis** and Pseudomonas syringae. These new domains are termed bacterial intein-like (BIL) domains. Bacterial intein-like domains are present in variable protein regions and are typically flanked by domains that also appear in secreted proteins such as filamentous haemagglutinin and calcium binding RTX repeats. Phylogenetic and genomic analysis of BIL sequences suggests that they were positively selected for in different lineages. We cloned two BIL domains of different types and showed them to be active. One of the domains efficiently cleaved itself from its C-terminal flank and could also protein-splice its two flanks, in E. coli and in a cell free system. We discuss several possible biological roles for BIL domains including microevolution and post translational modification for generating protein variability.

L7 ANSWER 4 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003072134 EMBASE
TITLE: Clinical evaluation of a DTaP-HepB-IPV combined **vaccine**.
AUTHOR: Partridge S.; Yeh S.H.
SOURCE: American Journal of Managed Care, (2003) 9/1 SUPPL. (S13-S22).
Refs: 23
ISSN: 1088-0224 CODEN: AJMCFY
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
007 Pediatrics and Pediatric Surgery
030 Pharmacology
038 Adverse Reactions Titles
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
036 Health Policy, Economics and Management
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective: To provide an overview of prelicensure clinical data for a new pediatric **vaccine** that combines diphtheria, tetanus,

acellular pertussis, hepatitis B, and inactivated poliovirus **vaccines** into a single injection (DTaP-HepB-IPV combined **vaccine**; Pediarix, GlaxoSmithKline Biologicals, Rixensart, Belgium). Methods: The safety and **immunogenicity** of DTaP-HepB-IPV combined **vaccine** have been evaluated extensively in clinical trials in infants. To date, DTaP-HepB-IPV combined **vaccine** has been administered to more than 7000 infants as a 3-dose primary series during the first year of life. Results: Studies show that DTaP-HepB-IPV combined **vaccine** is generally safe, well tolerated, and has not caused any significant serious adverse events. The rates of solicited and unsolicited reports of adverse reactions following **vaccination** were similar between groups receiving DTaP-HepB-IPV combined **vaccine** and comparator groups receiving the **vaccine** components separately. DTaP-HepB-IPV combined **vaccine** induces **immunogenicity** (as measured by seroprotection or **vaccine** response rates to each of the **vaccine** components [diphtheria, tetanus, 3 pertussis antigens, hepatitis B, and poliovirus types 1, 2, and 3]) similar to licensed **vaccine** components administered separately. Conclusion: In prelicensure clinical studies, DTaP-HepB-IPV combined **vaccine** was safe and **immunogenic** when given to infants as a primary 3-dose series. As a single injection of multiple **vaccine** components, DTaP-HepB-IPV combined **vaccine** may provide a safe and effective alternative to the current multiple-injection **immunization** regimen.

L7 ANSWER 5 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-058475 [05] WPIDS
CROSS REFERENCE: 2002-280437 [32]
DOC. NO. CPI: C2003-014970
TITLE: Novel diphtheria toxoid, tetanus toxoid and pertussis toxoid based combination **vaccine** for treating infections caused by Bordetella pertussis, Clostridium tetani, Corynebacterium diphtheriae or Hepatitis B virus.
DERWENT CLASS: B04 D16
INVENTOR(S): BOUTRIAU, D; CAPIAU, C; DESMONS, P M; LEMOINE, D; POOLMAN, J
PATENT ASSIGNEE(S): (GLAX) GLAXOSMITHKLINE BIOLOGICALS SA
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002080965	A2	20021017	(200305)*	EN	31

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2002080965 A2 WO 2002-EP3573 20020328

PRIORITY APPLN. INFO: GB 2001-8364 20010403
AN 2003-058475 [05] WPIDS
CR 2002-280437 [32]
AB WO 200280965 A UPAB: 20030121
NOVELTY - Multi-valent **vaccine** (I) against multiple pathogens comprising acellular pertussis components, tetanus and diphtheria toxoid, Hepatitis B surface antigen, inactivated polio virus and conjugates of carrier protein (P1) and/or capsular polysaccharide (P2) of Neisseria **meningitidis** type Y/C, or conjugates of P1 and P2 of Haemophilus influenzae type B and Streptococcus pneumoniae, is new.

DETAILED DESCRIPTION - A multi-valent **immunogenic** composition (I) for conferring protection in a host against disease caused by Bordetella pertussis, Clostridium tetani, Corynebacterium diphtheriae, Hepatitis B virus (HBV), Polio virus and Neisseria **meningitidis**, comprises acellular pertussis components having pertussis toxoid and filamentous hemagluttinin (**FHA**), tetanus toxoid (TT), diphtheria toxoid (DT), Hepatitis B surface antigen and inactivated polio virus, and either or both conjugates of a carrier protein and a capsular polysaccharide of a bacterium such as N.**meningitidis** type Y (MenY) or N. **meningitidis** type C (MenC), or for conferring protection in a host against disease caused by Haemophilus influenzae or Streptococcus pneumoniae comprises a conjugate of a carrier protein and the capsular polysaccharide of H.influenzae type B (Hib), and one or more conjugates of a carrier protein and a capsular polysaccharide from S.pneumoniae.

INDEPENDENT CLAIMS are also included for:

(1) a **vaccine** kit (II) for concomitant administration comprises two multi-valent **immunogenic** compositions for conferring protection in a host against disease caused by B.pertussis, C.tetani, C.diphtheriae, Hepatitis B virus, Polio virus and S.pneumoniae, where (II) comprises a first container comprising acellular pertussis components comprising pertussis toxoid and **FHA**, TT, DT, Hepatitis B surface antigen, and inactivated polio virus, and a second container comprising one or more conjugates of a carrier protein and a capsular polysaccharide from S.pneumoniae;

(2) making (M) (I) comprises mixing together the individual components; and

(3) a kit (III) comprising two multi-valent **immunogenic** compositions for conferring protection in a host against disease caused by B.pertussis, C.tetani, C.diphtheriae, Hepatitis B virus, Polio virus and N.**meningitidis**, H.influenzae and S.pneumoniae, comprises a first and second container comprising (I).

ACTIVITY - Antibacterial; Virucide.

MECHANISM OF ACTION - **Vaccine** (claimed).

The Haemophilus influenza type b (Hib-11) valent pneumococcal conjugate (Hib/Strep11V) **vaccine** and a control **vaccine** were administered in a three-dose (3, 4, 5 months of age) schedule to German infants. The immune response results (measured 1 month after the last primary administration) were as follows. The immune response, in terms of enzyme linked immunosorbent assay (ELISA) antibodies, of infants who received the

11Pn-PD/Hib **vaccine** was similar to that observed for those who received the 11Pn-PD **vaccine** for all of the serotypes, with the exception of serotypes 1,3 and 9V for which a trend to lower geometric mean concentrations was observed for the 11Pn-PD/Hib **vaccine**. However, these differences were not significant as shown by the overlapping of 95% confidence intervals. The 11Pn-PD/Hib **vaccine** induced functional (opsonophagocytic) antibodies to all 11 serotypes. Combining the Hib **vaccine** with the pneumococcal conjugate **vaccine** did not significantly interfere with the pneumococcal immune response and surprisingly enhanced the anti PRP (Hib polypeptide) response compared to both the registered **vaccines** Infanrix-HeXa and Hiberix.

USE - (I) is useful as a medicament or in the manufacture of a medicament for the treatment or prevention of diseases caused by infection by B.pertussis, C.tetani, C.diphtheriae, Hepatitis B virus, Polio virus, N.**meningitidis**, H.influenzae or S.pneumoniae, or for **immunizing** a human host against the above mentioned infections. (II) or (III) is useful for **immunizing** a human host against disease (claimed). (I) is useful for the manufacture of (II) or (III).

ADVANTAGE - (II) or (III) presents the various antigens to a host's immune system in an optimal manner. (II) or (III) provides the medical practitioner with an optimal method of **immunizing** a host with the following advantages: protective efficacy for all antigens, minimal reactogenicity, minimal carrier suppression interference, minimal adjuvant/antigen interference, or minimal antigen/antigen interference.

Dwg.0/0

L7 ANSWER 6 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-367614 [38] WPIDS
DOC. NO. CPI: C2001-112781
TITLE: **Immunogenic** composition for treating Neisserial bacteria infection, has Neisseria **meningitidis** antigens from serogroups B, C with further Neisserial proteins and protective antigens against other pathogenic organisms.
DERWENT CLASS: B04 D16
INVENTOR(S): GIULIANI, M M; PIZZA, M; RAPPUOLI, R
PATENT ASSIGNEE(S): (CHIR-N) CHIRON SPA
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001037863	A2	20010531	(200138)*	EN	27
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001018785	A	20010604	(200153)		
EP 1235589	A2	20020904	(200266)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					

BR 2000015958 A 20030225 (200320)
JP 2003514868 W 20030422 (200336) 43

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001037863	A2	WO 2000-IB1940	20001129
AU 2001018785	A	AU 2001-18785	20001129
EP 1235589	A2	EP 2000-981554	20001129
		WO 2000-IB1940	20001129
BR 2000015958	A	BR 2000-15958	20001129
		WO 2000-IB1940	20001129
JP 2003514868	W	WO 2000-IB1940	20001129
		JP 2001-539477	20001129

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001018785	A	Based on	WO 2001037863
EP 1235589	A2	Based on	WO 2001037863
BR 2000015958	A	Based on	WO 2001037863
JP 2003514868	W	Based on	WO 2001037863

PRIORITY APPLN. INFO: GB 1999-28196 19991129
AN 2001-367614 [38] WPIDS
AB WO 200137863 A UPAB: 20010711
NOVELTY - An **immunogenic** composition (I) comprising Neisseria **meningitidis** (Nm) serogroup C oligosaccharide and Nm serogroup B outer membrane protein, in combination with proteins (P1) (or its **immunogenic** fragments) and/or protective antigens against Nm serogroups A, W or Y, Hemophilus influenza, Pneumococcus, diphtheria, tetanus, whooping cough, hepatitis B virus and/or Helicobacter pylori, is new.

DETAILED DESCRIPTION - An **immunogenic** composition (I) comprising Neisseria **meningitidis** (Nm) serogroup C oligosaccharide and Nm serogroup B outer membrane protein, in combination with proteins (P1) (or its **immunogenic** fragments) and/or protective antigens against Nm serogroups A, W or Y, Hemophilus influenza, Pneumococcus, diphtheria, tetanus, whooping cough, hepatitis B virus and/or Helicobacter pylori, is new.

P1, or its **immunogenic** fragments, is disclosed in WO99/57280, WO99/36544, WO99/24578, WO97/28273, WO96/29412, WO95/03413 or WO99/31132.

INDEPENDENT CLAIMS are also included for the following:

(1) an **immunogenic** composition comprising NmC oligosaccharide and NmB proteins 919, 287 and/or ORF1; and

(2) a **vaccine** comprising (I).

ACTIVITY - Antibiotic.

MECHANISM OF ACTION - **Vaccine**.

Groups of guinea pigs received one of NmC conj./alum, NmB/alum, NmC conj./NmB/alum and NmC conj./NmB/MF59 **vaccine** components. Each animal received two injections, intramuscularly (IM), separated by 28 days. Serum samples were obtained prior to each injection and 18 days after the second injection. Each dose consisted of two 0.25 ml IM injections. Serum samples were assayed for IgG anticapsular antibody concentrations to NmC and for IgG

anti-outer membrane vesicle antibody concentrations to NmB by ELISA. A specific anti-**meningococcal** B antibody response was induced by the **vaccine** combinations comprising NmB and a specific anti-**meningococcal** C antibody response was induced by the **vaccine** combinations comprising NmC. The antibody response induced by the combination of NmC conjugate and NmB in the presence of MF59 adjuvant was significantly greater than the antibody response induced by either the NmC conjugate alone or the combination of the NmC conjugate and NmB in the presence of alum. When the adjuvant MF59 was present, the antibody titer for the combination **vaccine** increased approximately 6-fold. Serum samples were also tested for complement-mediated bactericidal titers to MenC strain 60E and MenB strain 44/76. The combination **vaccine** elicited high titers of serum bactericidal antibody for both NmB and NmC. 2-5 fold higher NmB bactericidal titers were obtained with the combination **vaccine** than with the NmB **vaccine** alone. The antibodies directed to **meningococcal** B and C induced by the **vaccine** combinations comprising NmB and NmC were bactericidal.

USE - (I) is useful for treating or preventing infection due to Neisserial bacteria.

Dwg.0/2

L7 ANSWER 7 OF 29 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2001454829 MEDLINE
DOCUMENT NUMBER: 21391802 PubMed ID: 11500415
TITLE: Production of Neisseria **meningitidis** transferrin-binding protein B by recombinant Bordetella pertussis.
AUTHOR: Coppens I; Alonso S; Antoine R; Jacob-Dubuisson F; Renauld-Mongenie G; Jacobs E; Locht C
CORPORATE SOURCE: Laboratoire de Microbiologie Genetique et Moleculaire, INSERM U447, Institut Pasteur de Lille, F-59019 Lille, France.
SOURCE: INFECTION AND IMMUNITY, (2001 Sep) 69 (9) 5440-6. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010814
Last Updated on STN: 20021218
Entered Medline: 20010913

AB Neisseria **meningitidis** serogroup B infections are among the major causes of fulminant septicemia and **meningitis**, especially severe in young children, and no broad **vaccine** is available yet. Because of poor **immunogenicity** of the serogroup B capsule, many efforts are now devoted to the identification of protective protein antigens. Among those are PorA and, more recently, transferrin-binding protein B (TbpB). In this study, TbpB of N. **meningitidis** was genetically fused to the N-terminal domain of the Bordetella pertussis **filamentous hemagglutinin** (**FHA**), and the **fha**-tbpB hybrid gene was expressed in B. pertussis either as a plasmid-borne gene or as a single copy inserted into the chromosome. The hybrid protein was efficiently secreted by the recombinant strains, despite its large size, and was recognized by

both anti-**FHA** and anti-TbpB antibodies. A single intranasal administration of recombinant virulent or pertussis-toxin-deficient, attenuated B. pertussis to mice resulted in the production of antigen-specific systemic immunoglobulin G (IgG), as well as local IgG and IgA. The anti-TbpB serum antibodies were of the IgG1, IgG2a, and IgG2b isotypes and were found to express complement-mediated bactericidal activity against N. **meningitidis**. These observations indicate that recombinant B. pertussis may be a promising vector for the development of a mucosal **vaccine** against serogroup B **meningococci**
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L7 ANSWER 8 OF 29 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001485587 MEDLINE
DOCUMENT NUMBER: 21418944 PubMed ID: 11528571
TITLE: A trial of acellular pertussis **vaccine** in hospital workers during the Cincinnati pertussis epidemic of 1993.
AUTHOR: Christie C D; Garrison K M; Kiely L; Gupta R K; Heubi J; Marchant C D
CORPORATE SOURCE: Divisions of Infectious Diseases and Epidemiology, Children's Hospital Medical Center, Cincinnati, OH, USA.. cchristi@jhsph.edu
CONTRACT NUMBER: RR-08084 (NCRR)
SOURCE: CLINICAL INFECTIOUS DISEASES, (2001 Oct 1) 33 (7) 997-1003.
Journal code: 9203213. ISSN: 1058-4838.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010903
Last Updated on STN: 20030105
Entered Medline: 20011204

AB The safety and **immunogenicity** of acellular pertussis (AP) **vaccine** in outbreak control was determined in a randomized, double-blind, controlled trial. Participants received AP **vaccine** (n=102), which contained 25 microg of pertussis toxoid (PT) and 3 microg of **filamentous hemagglutinin** (**FHA**), or licensed **meningococcal vaccine** (MN; n=97). Local reactions (pain or tenderness, redness, swelling, and induration) and systemic reactions (fever, sleepiness or lethargy, and irritability) were similar among AP and MN **vaccinees**. One month after AP **vaccination**, the geometric mean level of IgG anti-PT was 33.1 microg/mL, with 2-fold increases in 85% of patients and 4-fold increases in 73% of patients; for IgG anti-**FHA**, the respective values were 34.7 microg/mL, 92%, and 63%. After 6 months of follow-up, no serological evidence of pertussis was seen among symptomatic or asymptomatic subjects. However, recent evidence of Bordetella pertussis infection before **immunization** was shown. Thus, AP **vaccine** was safe and **immunogenic** in adults.

L7 ANSWER 9 OF 29 EMBASE

RESERVED. on STN DUPLICATE 3
ACCESSION NUMBER: 2001299839 EMBASE
TITLE: Genetic analysis of virulence factors of Mannheimia (Pasteurella) haemolytica A1.
AUTHOR: Lo R.Y.C.
CORPORATE SOURCE: R.Y.C. Lo, Department of Microbiology, University of Guelph, Guelph, Ont. N1G 2W1, Canada. rlo@micro.uoguelph.ca
SOURCE: Veterinary Microbiology, (22 Oct 2001) 83/1 (23-35). Refs: 39
ISSN: 0378-1135 CODEN: VMICDQ
PUBLISHER IDENT.: S 0378-1135(01)00374-1
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Using a molecular genetic approach, the genes that code for the various virulence factors of Mannheimia haemolytica A1 have been cloned for detailed characterizations. These included analysis of the encoded proteins, their biological activities, secretion of the molecules from the bacterium as well as their use in a **vaccine** component. Two newly characterized antigens of M. haemolytica A1 have been identified. The first one is a TonB-dependent iron regulated outer-membrane receptor that is distinct from the transferrin binding proteins. The 84 kDa Irp protein exhibits features including a TonB box and a 50 amino acid region that can adopt occluded β-barrel structures similar to the "plug" domain of the Escherichia coli FhuA and FepA crystal structures. Homologues of Irp were identified by analysis of the genome sequences of a number of Gram negative mucosal pathogens, including Neisseria **meningitidis** and N. gonorrhoeae. The Neisserial irp genes were cloned by PCR and expressed the 84 kDa protein as expected, demonstrating that they are functional genes. In addition to being regulated by iron and Fur, irp(Mh) undergoes phase variation by a slipped-strand mispairing mechanism and may represent a contingency locus for iron acquisition during an infection. Another locus that codes for a putative adhesin molecule has also been partially characterized. This putative adhesin protein is highly homologous with the high-molecular-weight adhesin proteins of non-piliated non-typable strains of Haemophilus influenzae (NTHi) including Hia, Hsf, HMW1, HMW2. Currently, we have cloned the DNA that codes for 2223 amino acids (225 kDa) and is still missing the stop codon. It is anticipated that when complete, the protein could be close to 240 kDa, similar to the molecular mass of Hsf. Though incomplete, analysis of the adhesin showed that it exhibits characteristics of autotransporter (AT) proteins. The role of this high-molecular-weight adhesin in infection is being investigated.

L7 ANSWER 10 OF 29 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2000096659 MEDLINE
DOCUMENT NUMBER: 20096659 PubMed ID: 10629468
TITLE: Effect of acellular pertussis **vaccine** on the development of allergic sensitization to environmental allergens in adults.
AUTHOR: Assa'ad A; Lierl M
CORPORATE SOURCE: Division of Pulmonary Medicine, Allergy and Clinical

Immunology, Children's Hospital Medical Center, Cincinnati, OH 45229, USA.
SOURCE: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (2000 Jan) 105 (1 Pt 1) 170-5.
Journal code: 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000218
Entered Medline: 20000208

AB BACKGROUND: Exposure of children to pertussis antigens caused by infection or **vaccination** with whole-cell pertussis **vaccine** may increase the serum IgE level and predispose to sensitization to the prevalent environmental allergens. Acellular pertussis **vaccine** (APV) that may be given to adults may have a similar effect. OBJECTIVE: The purpose of this study was to determine whether APV will cause an increase in environmental sensitization measured by an increase of serum-specific IgE to the allergens to which adults are exposed during the **vaccination** period. METHODS: One hundred adult hospital employees were randomized to receive either a 2-component APV composed of pertussis toxin and **filamentous hemagglutinin** or a **meningococcal vaccine** as a control. Serum-specific IgE level to 2 indoor allergens, cat and dust mite, and 2 outdoor allergens prevalent during the **immunization** season, Alternaria species and ragweed, was measured by an RIA on sera collected before and 1 month after **vaccination.** RESULTS: The group that received the APV had no significant change in their serum-specific IgE levels to cat, dust, Alternaria species, or ragweed 1 month after **vaccination.** CONCLUSION: A 2-component APV did not predispose to an increase of allergen-specific IgE in an adult population.

L7 ANSWER 11 OF 29 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2000134026 MEDLINE
DOCUMENT NUMBER: 20134026 PubMed ID: 10670566
TITLE: A nasal whole-cell pertussis **vaccine** induces specific systemic and cross-reactive mucosal antibody responses in human volunteers.
AUTHOR: Berstad A K; Holst J; Froholm L O; Haugen I L; Wedege E; Oftung F; Haneberg B
CORPORATE SOURCE: Department of Vaccinology, National Institute of Public Health, Oslo, Norway.
SOURCE: JOURNAL OF MEDICAL MICROBIOLOGY, (2000 Feb) 49 (2) 157-63.
Journal code: 0224131. ISSN: 0022-2615.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000309

Last Updated on STN: 20021218
Entered Medline: 20000222

AB A whole-cell pertussis **vaccine**, each dose consisting of 250 microg of protein, was given intranasally four times at weekly intervals to six adult volunteers. All **vaccinees** responded with increases in nasal fluid IgA antibodies to Bordetella pertussis whole-cell antigen. Three **vaccinees** with high nasal antibody responses also developed increased serum IgA and IgG antibodies to this antigen. Salivary antibody responses to the whole-cell antigen, as well as antibodies in serum and secretions to pertussis toxin (PT) and filamentous haemagglutinin (**FHA**) were negligible, except for a moderate increase in nasal fluid antibodies to **FHA**. Unexpectedly, the same **vaccinees** developed significant rises in nasal and salivary IgA antibodies to **meningococcal** outer-membrane antigens, whereas corresponding serum IgA and IgG antibodies were unchanged. Thus it appears that mucosal **immunisation** may induce secretory antibodies with broader specificities than can be found in serum.

L7 ANSWER 12 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-580365 [49] WPIDS
DOC. NO. CPI: C1999-168834
TITLE: Reducing interference from Haemophilus polysaccharide component in combined **vaccines** against diphtheria, tetanus and pertussis.
DERWENT CLASS: B04
INVENTOR(S): ARTOIS, C; DE HEYDER, K; DESMONS, P; GARCON, N; MAINIL, R; HEYDER, K D
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9948525	A1	19990930	(199949)*	EN	35
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9934172	A	19991018	(200009)		
NO 2000004758	A	20001108	(200067)		
BR 9909037	A	20001205	(200101)		
EP 1066053	A1	20010110	(200103)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI					
CN 1295481	A	20010516	(200146)		
AU 735619	B	20010712	(200147)		
CZ 2000003536	A3	20010815	(200157)		
HU 2001001323	A2	20010828	(200157)		
KR 2001034630	A	20010425	(200164)		
MX 2000009378	A1	20010301	(200170)		
JP 2002507581	W	20020312	(200220)		44
ZA 2000004956	A	20020227	(200223)		50
US 2003022304	A1	20030130	(200311)		
NZ 506604	A	20030228	(200323)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9948525	A1		WO 1999-EP1959	19990322
AU 9934172	A		AU 1999-34172	19990322
NO 2000004758	A		WO 1999-EP1959	19990322
			NO 2000-4758	20000922
BR 9909037	A		BR 1999-9037	19990322
			WO 1999-EP1959	19990322
EP 1066053	A1		EP 1999-915692	19990322
			WO 1999-EP1959	19990322
CN 1295481	A		CN 1999-804445	19990322
AU 735619	B		AU 1999-34172	19990322
CZ 2000003536	A3		WO 1999-EP1959	19990322
			CZ 2000-3536	19990322
HU 2001001323	A2		WO 1999-EP1959	19990322
			HU 2001-1323	19990322
KR 2001034630	A		KR 2000-710518	20000922
MX 2000009378	A1		MX 2000-9378	20000925
JP 2002507581	W		WO 1999-EP1959	19990322
			JP 2000-537572	19990322
ZA 2000004956	A		ZA 2000-4956	20000918
US 2003022304	A1	Cont of	WO 1999-EP1959	19990322
		Cont of	US 2000-647032	20001031
			US 2002-217572	20020813
NZ 506604	A		NZ 1999-506604	19990322
			WO 1999-EP1959	19990322

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9934172	A	Based on	WO 9948525
BR 9909037	A	Based on	WO 9948525
EP 1066053	A1	Based on	WO 9948525
AU 735619	B	Previous Publ.	AU 9934172
		Based on	WO 9948525
CZ 2000003536	A3	Based on	WO 9948525
HU 2001001323	A2	Based on	WO 9948525
JP 2002507581	W	Based on	WO 9948525
NZ 506604	A	Based on	WO 9948525

PRIORITY APPLN. INFO: GB 1998-6456 19980325
AN 1999-580365 [49] WPIDS
AB WO 9948525 A UPAB: 19991124
NOVELTY - Reducing interference of a capsular polysaccharide component of a conjugated Haemophilus influenzae B **vaccine** (Hib) in a combined **vaccine** containing diphtheria and tetanus toxoids and acellular pertussis components (DTPa).

DETAILED DESCRIPTION - Reducing interference of a capsular polysaccharide component of a conjugated Haemophilus influenzae B **vaccine** (Hib) in a combined **vaccine** containing diphtheria and tetanus toxoids and acellular pertussis components (DTPa) comprises:

(a) pre-saturating aluminum hydroxide (AH) adjuvant with one or more selected antigens;

(b) selecting Hib and one or more additional antigens to be adsorbed on to aluminum phosphate (AP) adjuvant; and

(c) combining all the antigens.

An INDEPENDENT CLAIM is also included for a combined **vaccine** prepared this way.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Induction of specific immune responses.

USE - The method is used to prepare **vaccines** for preventing infection by diphtheria, tetanus, pertussis and H. influenzae, particularly in children.

ADVANTAGE - This method of **vaccine** preparation avoids interference from Hib while maintaining the maximum, stable activity of all antigens on their preferred adjuvant. Especially pertussis antigens are stably retained in their most potent form and Hib remians immunologically active for a long period. The method does not require addition of anions (contrast the method of WO 963722) and presaturation of AH means that the dose of potentially reactogenic AH can be reduced.

Dwg.0/0

L7 ANSWER 13 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-443571 [37] WPIDS
CROSS REFERENCE: 1998-456074 [39]; 1999-600812 [51]; 2000-181133 [16]
DOC. NO. CPI: C1999-130580
TITLE: Peptides inhibiting the adhesion between leukocytes and endothelial cells, useful for treating inflammation.
DERWENT CLASS: B04
INVENTOR(S): MASURE, H R; TUOMANEN, E
PATENT ASSIGNEE(S): (UYRQ) UNIV ROCKEFELLER
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5932217	A	19990803	(199937)*		82

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 5932217	A	CIP of	US 1991-695613	19910503
		CIP of	WO 1992-US3725	19920504
		CIP of	US 1994-247572	19940523
		CIP of	US 1994-140136	19940714
			US 1994-348353	19941130

PRIORITY APPLN. INFO: US 1994-348353 19941130; US 1991-695613 19910503; WO 1992-US3725 19920504; US 1994-247572 19940523; US 1994-140136 19940714
AN 1999-443571 [37] WPIDS
CR 1998-456074 [39]; 1999-600812 [51]; 2000-181133 [16]
AB US 5932217 A UPAB: 20000330
NOVELTY - Peptides which inhibit adhesion between leukocytes and endothelial cells, are new.

DETAILED DESCRIPTION - The peptides comprise:

IGALKAGAVEAASPRRARRALRQDFFTPGSVVVRAQGNVTVGRGDP (I); RQDFFTPGSVVVRAQGNVTVTRGDPMQGVLAQDIIMDAKGGTLL (II); RGDPMQGVLAQGDIIMDAKGGTLLLRNDALTEMGTVTISADSAVL (III); RGDPHQGVLAQGDIIMDAKG (IV); ETKEVDG (V); GRTRG (VI); GLIQGRSVKVD (VII); LGYQAIC (VIII); and LEHSTIESSKISQSVLAAKGDKGKPAVSUKVAKKLFLNGTL RAVND (IX).

INDEPENDENT CLAIMS are also included for the following:

(1) a peptide which inhibits adhesion between bacteria (Bordetella pertussis) and cilliated respiratory epithelial cells, where the peptide is (IX); AKKLFLNGTLRAVNDNNETMSGRQIDVVDGRPQITDAVTGE ARKD (X); GRPQITDAVTGEARKDESVVSDAALVADGGPIVVEAGELVSHAGGIG (XI); IVVEAGELVSHAGGIGNGRNKENGASVTVRTTGNLVNKGYISHG (XII); MQGVLAQGDIIMDAKGGTLLLRNDALT (XIII); or PMQGVLAQGDIIMDAKGGTLLLRNDALTE MSTVTISADSAVL (XIV);

(2) a composition useful for inhibiting the influx of leukocytes into inflamed tissue comprising a peptide selected from (I); RQDFFTPGSVVVRAQGNVTVTRGDPMQGVLAQGDIIMDAKGGTLL (XV); or RGDPMGGVLAQGDIIMDAKGGTLLRNDALTEMGTVTISADSAVL (XVI); and

(3) an **immunogenic** composition comprising a polypeptide portion of Bordetella pertussis **filamentous hemagglutin** (**FHA**) containing no RGD region or containing an amino acid sequence altered in the RGD region, where the polypeptide portion elicits antibodies which do not cross-react with cerebral endothelial cells.

ACTIVITY - Anti-inflammatory.

MECHANISM OF ACTION - Prevent leukocyte binding to endothelial cells.

The ability of **FHA** peptides and anti-CD18 or anti-Factor X receptor antibodies to interact cooperatively to inhibit neutrophil adherence to endothelial cells was assessed by measuring neutrophil adherence to endothelial cells in the presence of antibody as well as antibody plus peptide. Anti-CD18 mAb IB4 was added to leukocytes at 10 micro g/ml 10 min before the assay. Anti-factor X receptor mAb 12H1 or 9D4 were added to the endothelial cell monolayers 10 min before the assay. The peptides were added at 5 micro g/ml. In control wells, 228 neutrophils were adherent per 40 multiply field. Maximum inhibition of antibody or peptide alone was 40-60% of control values. Preincubation of neutrophils with **FHA** peptides LGYQAK or GYDTKQEDG together with the anti-CD18 mAb IB4 resulted in an additive reduction of neutrophil adherence to greater than 80%.

USE - The peptides and methods are useful for reducing inflammation during the course of antibiotic therapy of infectious diseases such as **meningitis**, septic arthritis, and endophathalmitis.

Dwg.0/31

L7 ANSWER 14 OF 29 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 1999210722 MEDLINE
DOCUMENT NUMBER: 99210722 PubMed ID: 10194818
TITLE: New acellular pertussis-containing paediatric combined **vaccines**.
AUTHOR: Pines E; Barrand M; Fabre P; Salomon H; Blondeau C; Wood S C; Hoffenbach A
CORPORATE SOURCE: Pasteur Merieux Connaught, Marnes-la Coquette, France.
SOURCE: VACCINE, (1999 Mar 26) 17 (13-14) 1650-6. Ref: 51
Journal code: 8406899. ISSN: 0264-410X.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990527

AB Combined pediatric **vaccines** have the advantages of conferring protection against multiple common infectious diseases with a reduced number of injections. Their use should lead to better compliance to recommended **vaccination** schedules. Diphtheria (D), tetanus (T) and whole-cell pertussis **vaccine** (P) have been successfully combined, with or without inactivated poliovirus **vaccine** (IPV) in the same syringe for many years. Recently developed acellular pertussis (aP) Haemophilus influenzae type B (Hib), inactivated poliomyelitis virus and hepatitis B **vaccines** are ideal candidates for inclusion in current combined **vaccines**. Nevertheless, the development of new combinations has to face preclinical and clinical issues: the appropriate formulation of the new antigen(s) and other **vaccine** components needs to be determined to ensure compatibility and guard against potential additive or unexpected adverse reactions; potential immunological interference between antigens and the negative impact of other **vaccine** components on **immunogenicity** may occur, and these have to be examined also. Whole-cell pertussis **vaccines** are highly protective against whooping cough, but the severe adverse reactions that these **vaccines** sometimes produce have led to hesitation over their use, including the decision of some countries to stop pertussis **immunization**. To increase the acceptability of pertussis **vaccination**, Pasteur Merieux Connaught has developed a combined D, T and a two-component acellular pertussis **vaccine** (DTaP), composed of purified pertussis toxoid (PT) and filamentous haemagglutinin (**FHA**), which has been shown to be effective in an efficacy trial conducted in Senegal. Acellular DTaP **vaccines** are **immunogenic** and have a better safety profile than DTP **vaccines**, when given either for the primary series, for the booster **vaccination** or for both. In order to meet worldwide demands, the combined DTaP-IPV or DTP-IPV has been developed for countries where IPV is recommended. Following the encouragement of the WHO, an H. influenzae type B tetanus-conjugated (Act-HIB) **vaccine**, has been combined in a full liquid formulation with the whole-cell DTP. This **vaccine** showed a good safety and **immunogenicity** profile in infants and in toddlers. A combined DTaP-IPV-PRP-T **vaccine** (where the Act-HIB **vaccine** is reconstituted by the full-liquid DTaP-IPV) also has been successfully developed both for the primary series and for booster **vaccination**; although, a reduced **immunogenicity** against PRP observed after the primary series, this did not affect **vaccine** priming. Hepatitis B **immunization** campaigns targeting high-risk groups have failed to control the disease in areas of low endemicity. In 1992, the WHO recommended that hepatitis B **vaccination** should be integrated into the EPI in all countries by 1997-1999. For that

purpose, hepatitis B **vaccine** is currently evaluated in pediatric combined **vaccines**. Developing new combination **vaccines** is a difficult but essential process for maintaining high **immunization** rates worldwide against infectious diseases, provided that the costs are acceptable. New combined **vaccines** including pneumococcal and **meningococcal** component are under wide-scale development.

L7 ANSWER 15 OF 29 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1999:224743 SCISEARCH
THE GENUINE ARTICLE: 175YG
TITLE: Safety and **immunogenicity** of combined diphtheria tetanus pertussis (whole cell and acellular) Haemophilus influenzae b conjugate **vaccines** administered to Indonesian children
AUTHOR: Richie E; Punjabi N H; Harjanto S J; Wangsasaputral F; Sukandar M; Supriatman M; Simanjuntak C H; Que J U; Cryz S J (Reprint)
CORPORATE SOURCE: SWISS SERUM & VACCINE INST, REHHAGSTR 79, CH-3018 BERN, SWITZERLAND (Reprint); SWISS SERUM & VACCINE INST, CH-3018 BERN, SWITZERLAND; USN, MED RES UNIT 2, JAKARTA 10560, INDONESIA; NATL INST HLTH RES & DEV, JAKARTA 10560, INDONESIA
COUNTRY OF AUTHOR: SWITZERLAND; INDONESIA
SOURCE: VACCINE, (17 MAR 1999) Vol. 17, No. 11-12, pp. 1384-1393.
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.
ISSN: 0264-410X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; AGRI
LANGUAGE: English
REFERENCE COUNT: 37

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A randomized, double-blind trial was conducted to evaluate the safety and **immunogenicity** of **vaccines** comprised of diphtheria to) and tetanus (T) toxoids combined with either a whole cell (P) or an acellular (aP) pertussis component and Haemophilus influenzae type b polyribosylphosphate (PRP)-tetanus toroid conjugate (PRP-T) in Indonesian infants. Three doses of either DTaP, DTaP-PRP-T, or DTP-PRP-T were administered to 930 infants approximately 2-3 months of age and at 2 month intervals thereafter. A booster dose of either DTP-PRP-T or DTaP-PRP-T was administered at 15-18 months of age, Both local and systemic reactions occurred at a significantly (p less-than 0.001-0.026) higher rate in the group that received whole cell pertussis **vaccine** versus groups which were **immunized** with aP containing **vaccines**. There was no significant difference (p greater-than 0.05) in the rate of adverse events between groups **immunized** with DTaP or DTaP-PRP-T. One month after the third dose of **vaccine**, 99% of subjects had achieved greater than or equal to 0.1 IU of anti-D and anti-T antibody per ml of serum. The geometric mean titer (GMT) to D was significantly (p less-than 0.001) higher in the group **immunized** with DTaP versus the other two groups whereas the anti-T GMT was significantly(p less-than 0.006) higher for the group **immunized** with DTP-PRP-T. Both the anti-pertussis toxin (PT) and anti-**filamentous hemagglutinin** (**FHA**) antibody

levels were significantly (p less-than 0.001) higher in recipients of acellular versus whole cell pertussis **vaccine**. In contrast, the anti-B. pertussis agglutinating antibody response was significantly(p less-than 0.0001) higher in the group **immunized** with whole cell pertussis **vaccine**. The anti-PRP GMTs (mu g antibody/ml) at 7 months were 0.096, 3.35 and 6.11 for groups **immunized** with DTaP, DTaP-PRP-T and DTP-PRP-T. respectively. The GMT for those **immunized** with DTP PRP-T was significantly (p less-than 0.001) higher compared to recipients of DTaP-PRP-T. The percent of children who attained greater than or equal to 0.15 or greater than or equal to 1 mu g/ml after **immunization** was 18 and 2% for the DTaP group, 93 and 76% for the DTaP-PRP-T group and 97 and 88% for the DTP PRP-T group. At the greater than or equal to 1 mu g/ml level the difference between the DTaP-PRP-T and DTP-PRP-T groups was significant (p less-than 0.01). Children **immunized** with either DTaP, DTaP-PRP-T. or DTP-PRP-T were reimmunized with DTaP-PRP-T whereas. a portion of children **immunized** with DTP-PRP-T where also boosted with this **vaccine** at 15-18 months of age.

There was a vigorous anamnestic response to the D and T components with all children possessing greater than or equal to 0.1 IU/ml. There was also a substantial increase in anti-PT, anti-**FHA** and B, pertussis agglutinating antibodies. The poorest anti-PT response was seen among children receiving DTP-PRP-T for both primary and reimmunization while the highest agglutinating antibody response followed receipt of 4 doses of DTP-PRP-T. Greater than 80% of children **immunized** with either DTP-PRP-T dr DTaP-PRP-T possessed greater than or equal to 0.15 mu g/ml before boosting versus 38% for those **vaccinated** with DTaP (p less-than 0.001). Primary **immunization** with DTP-PRP-T resulted in a significantly (p less-than 0.05) higher percentage (72%) maintaining greater than or equal to 1 mu g/ml compared to those **immunized** with DTaP PRP-T (46%). Prior to reimmunization, the anti-PRP GMT was significantly (p less-than 0.005) higher for children **immunized** with 3 doses of DTP-PRP-T versus DTaP-PRP-T Subsequent to reimmunization. greater than or equal to 95% of subjects attained greater than or equal to 1 mu g/ml.

L7 ANSWER 16 OF 29 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 1999421077 MEDLINE
DOCUMENT NUMBER: 99421077 PubMed ID: 10493334
TITLE: Safety and **immunogenicity** of heptavalent pneumococcal CRM197 conjugate **vaccine** in infants and toddlers.
AUTHOR: Shinefield H R; Black S; Ray P; Chang I; Lewis N; Fireman B; Hackell J; Paradiso P R; Siber G; Kohberger R; Madore D V; Malinowski F J; Kimura A; Le C; Landaw I; Aguilar J; Hansen J
CORPORATE SOURCE: Kaiser Permanente Pediatric Vaccine Study Center of Northern California, Oakland, USA.. henry.shinefield@kp.org
SOURCE: PEDIATRIC INFECTIOUS DISEASE JOURNAL, (1999 Sep) 18 (9) 757-63.
Journal code: 8701858. ISSN: 0891-3668.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991202

AB OBJECTIVES: The objectives of this study were (1) to determine the safety and **immunogenicity** of heptavalent pneumococcal CRM197 conjugate (PNCRM7) **vaccine** in infants and (2) to determine the effect of concurrent hepatitis B **immunization** during the primary series and the effect of concurrent diphtheria and tetanus toxoid and acellular pertussis [DTaP (ACEL-IMUNE)] and conjugate CRM197 Haemophilus influenzae type b [HbOC (HibTITER) **immunization** at time of the booster dose on the safety and **immunogenicity** of PNCRM7and these other concurrently administered **vaccines**. METHODS: This was a randomized double-blinded study in 302 healthy infants in the Northern California Kaiser Permanente (NCKP) Health Plan. Infants received either PNCRM7 **vaccine** or **meningococcal** group C conjugate **vaccine** as a control at 2, 4 and 6 months of age and a booster at 12 to 15 months of age. Study design permitted the evaluation of immunology and safety of concurrent administration of routine **vaccines**. Antibody titers were determined on blood samples drawn before and 1 month after the primary series and the booster dose. RESULTS: After the third dose of PNCRM7 geometric mean concentrations (GMCs) ranged from 1.01 for serotype 9V to 3.72 microg/ml for serotype 14. More than 90% of all subjects had a post-third dose titer of > or =0.15 microg/ml for all serotypes, and the percentage of infants with a post-third dose titer of > or =1.0 microg/ml ranged from 51% for type 9V to 89% for type 14. After the PNCRM7 booster dose, the GMCs of all seven serotypes increased significantly over both post-Dose 3 and pre-Dose 4 antibody levels. In the primary series there were no significant differences in GMCs of pneumococcal antibodies between the subjects given PN-CRM7 alone or concurrently with hepatitis B **vaccine**. At the toddler dose concurrent administration of PNCRM7 and DTaP and HbOC resulted in a near conventional threshold for statistical significance of a post-Dose 4 GMC for serotype 23F [alone 6.75 mirog/ml vs. concurrent 4.11 microg/ml (P = 0.057)] as well as significantly lower antibody GMCs for H. influenza polyribosylribitol phosphate, diphtheria toxoid, pertussis toxin and **filamentous hemagglutinin**. For all antigens there were no differences between study groups in defined antibody titers that are considered protective. CONCLUSION: We conclude that PNCRM7 **vaccine** was safe and **immunogenic**. When this **vaccine** was administered concurrently at the booster dose with DTaP and HbOC **vaccines**, lower antibody titers were noted for some of the antigens when compared with the antibody response when PNCRM7 was given separately. Because the GMCs of the booster responses were all generally high and all subjects achieved similar percentages above predefined antibody titers, these differences are probably not clinically significant.

L7 ANSWER 17 OF 29 EMBASE on STN
ACCESSION NUMBER: 1999035998 EMBASE

TITLE: Viral influenza in women.
AUTHOR: Rhoton-Vlasak A.
CORPORATE SOURCE: Dr. A. Rhoton-Vlasak, Department of Obstetrics/Gynecology, Repro. Endocrinol./Infertility Div., University of Florida, P.O. Box 100294, Gainesville, FL 32610-0294, United States
SOURCE: Primary Care Update for Ob/Gyns, (1999) 6/1 (1-7).
Refs: 11
ISSN: 1068-607X CODEN: PUOGEP
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Viral influenza is an acute respiratory infection caused by strains of the orthomyxovirus. The influenza viruses are negative-stranded RIVA viruses of three major antigenic types-A, B, and C. Influenza A and B viruses are most important in human disease and have been studied far more extensively than influenza C viruses. Influenza A and B viruses are characterized based on their hemagglutinin and neuraminidase antigens. Immunity to these antigens, especially to the hemagglutinin, reduces the likelihood of infection and lessens the severity of disease if infection occurs. Because of this antigenic variation, major epidemics of respiratory disease caused by new variants of influenza continue to occur. The antigenic characteristics of circulating strains provide the basis for selecting the virus strains included in each year's **vaccine** . Viral influenza may cause serious morbidity, especially in adults, and result in prolonged absences from work. Mortality may occur as a result of secondary infection with bacterial pneumonia or other complications, such as myocarditis, pericarditis, aseptic **meningitis**, and postinfection neuritis. Two measures available that can reduce the impact of influenza are immunoprophylaxis with inactivated **vaccine** and chemoprophylaxis or therapy with an antiviral drug such as amantadine or rimantadine. Intensive supportive therapy with antipyretics, analgesics, and fluid repletion also is important. Nonpregnant patients may be treated with amantadine to reduce the severity of symptoms. Amantadine or rimantadine are relatively contraindicated in pregnancy. The best method of prevention in pregnant women is the influenza **vaccine**.

L7 ANSWER 18 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 95174991 EMBASE
DOCUMENT NUMBER: 1995174991
TITLE: Hypothesis: Serum IgG antibody is sufficient to confer protection against infectious diseases by inactivating the inoculum.
AUTHOR: Robbins J.B.; Schneerson R.; Szu S.C.
CORPORATE SOURCE: Devtl./Molecular Immunity Laboratory, Bldg. 6, NIH,Bethesda, MD 20892, United States
SOURCE: Journal of Infectious Diseases, (1995) 171/6 (1387-1398).

ISSN: 0022-1899 CODEN: JIDIAQ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The theory proposed is that a critical level of specific serum IgG is sufficient to confer protection against infectious diseases by inactivating the inoculum of the pathogen. This theory relies heavily on evaluation of licensed **vaccines** and includes the following: Measurement of serum antibodies only reliably predicts the efficacy of **vaccines**, according to regulatory agencies. Serum IgG antibodies alone account for the protection conferred by passive **immunization**. 'Herd' immunity conferred by **vaccines** on viral and bacterial diseases is best explained by serum antibodies that inactivate the inoculum on mucosal surfaces, thus reducing the pathogen's transmission. Once the disease is manifest, serum antibodies induced by active **immunization** will neither relieve symptoms nor eliminate the pathogen; specific IgG must be present when the host encounters the pathogen in order to confer protective immunity. Information about the initial pathogen-host contact is vital, whereas knowledge of the symptomatology of the disease may not be essential for **vaccine** development.

L7 ANSWER 19 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1995:525955 BIOSIS
DOCUMENT NUMBER: PREV199598540255
TITLE: Safety and **immunogenicity** in adolescents of BIOCINE 3 component acellular pertussis **vaccine** (aP) containing a genetically detoxified pertussis toxin.
AUTHOR(S): Mink, C. M. (1); Rothstein, E.; Forrest, B. D.; Izu, A.; Sinangil, F.; Duane, C.; Bernstein, H. H.; Granoff, D. M.
CORPORATE SOURCE: (1) St. Louis Univ., MO USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1995) Vol. 35, No. 0, pp. 163.
Meeting Info.: 35th Interscience Conference on Antimicrobial Agents and Chemotherapy San Francisco, California, USA September 17-20, 1995
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 20 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 8
ACCESSION NUMBER: 93231172 EMBASE
DOCUMENT NUMBER: 1993231172
TITLE: Haemophilus influenzae type b polysaccharide-tetanus protein conjugate **vaccine** does not depress serologic responses to diphtheria, tetanus or pertussis antigens when coadministered in the same syringe with diphtheria- tetanus-pertussis **vaccine** at two, four and six months of age.

AUTHOR: Avendano A.; Ferreccio C.; Lagos R.; Horwitz I.; Cayazzo M.; Fritzell B.; Meschievitz C.; Levine M.
CORPORATE SOURCE: Center for Vaccine Development, Maryland University Sch. of Medicine, 10 S. Pine St.,Baltimore, MD 21201, United States
SOURCE: Pediatric Infectious Disease Journal, (1993) 12/8 (638-643).
ISSN: 0891-3668 CODEN: PIDJEV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The safety and **immunogenicity** of a **vaccine** against Haemophilus influenzae type b consisting of purified polyribosylribitol phosphate conjugated to tetanus toxoid (PRP-T) were evaluated in 277 Chilean infants who were randomly assigned to one of three treatment groups: Group A, PRP-T mixed with diphtheria-tetanus-pertussis (DTP) **vaccine** in a single syringe and given as a single inoculation in one arm and placebo in the other arm; Group B, PRP-T given in one arm and DTP in the other arm; Group C, DTP given in one arm and placebo in the other. Infants were **immunized** at 2, 4 and 6 months of age and examined daily for 4 days after each **immunization**. Serum PRP antibodies; tetanus, diphtheria and pertussis antitoxin; pertussis agglutinins; and antibodies to Bordetella pertussis **filamentous hemagglutinin** were measured at baseline and 2 months after each dose. PRP-T was well-tolerated. After three doses of PRP-T **vaccine** 100% of infants attained PRP antibody concentrations ≥0.15 μg/ml and 96 to 99% achieved high anti-PRP concentrations (≥1.0 μg/ml). The post-third dose anti-PRP geometric mean titer was high (6.94 μg/ml) in infants who were given PRP-T combined with DTP, although it was somewhat lower than the geometric mean titer of the group who received PRP-T in a separate arm (9.93 μg/ml) (P not significant). No differences were detected among the groups in tetanus antitoxin response, whereas after two or three doses the geometric mean titer of diphtheria antitoxin was significantly higher in the group who received PRP-T combined with DTP than in the group who received PRP-T as a separate inoculation ($P < 0.016$). Pertussis agglutinin, antitoxin and anti-**filamentous hemagglutinin** responses did not differ among the groups. These results encourage coadministration of PRP-T and DTP in a single inoculation, in view of the practical advantages of such combined **immunization**.

ACCESSION NUMBER: 93002966 EMBASE
DOCUMENT NUMBER: 1993002966
TITLE: Susceptibility to measles virus-induced encephalitis in mice correlates with impaired antigen presentation to cytotoxic T lymphocytes.
AUTHOR: Niewiesk S.; Brinckmann U.; Bankamp B.; Sirak S.; Liebert U.G.; Ter Meulen V.

CORPORATE SOURCE: Molecular Immunology Group, Institute of Molecular Medicine, John Radcliffe Hospital,Headington, Oxford OX3 9DU, United Kingdom
SOURCE: Journal of Virology, (1993) 67/1 (75-81).
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In measles virus (MV) infection in humans, **meningitis** and encephalitis are important complications. However, little is known of the pathogenesis of MV encephalitis, in particular about the role of the immune response. We have examined the role of cytotoxic T lymphocytes (CTL) in a mouse model of MV- induced encephalitis. We report here that the resistance of inbred strains of mice to MV-induced encephalitis correlated with the major histocompatibility complex (MHC) haplotype and that only resistant mouse strains mounted an effective CTL response to MV. Mice with low susceptibility to MV infection, such as the BALB/c strain (H-2(d)), generated CTL, whereas the highly susceptible strains, C3H (H-2(k)) and C57BL/6 (H-2b), revealed very poor CTL responses. MV-induced CTL were usually CD8+, and the generation of these cells was independent of the route of inoculation or the time postinfection. CD4+ T cells were generally only weakly lytic. The nucleocapsid protein was the major target antigen for CTL in BALB/c mice, although in some experiments the hemagglutinin was also recognized. CTL from C3H and C57BL/6 mice did not lyse MV-infected target cells. However, targets infected with **vaccinia** virus recombinants expressing the nucleocapsid protein or hemagglutinin were lysed, but levels of cytotoxicity were still low. Experiments using target cells transfected with single MHC class I genes suggested inefficient antigen presentation of MV proteins by the MHC molecules of the H-2(k) and H-2b haplotypes.

L7 ANSWER 22 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:467088 BIOSIS
DOCUMENT NUMBER: PREV199345090213
TITLE: Envelope structure and the development of new **vaccines**.
AUTHOR(S): Robinson, A. (1); Melling, J.
CORPORATE SOURCE: (1) Div. Biol., PHLS Cent. Applied Microbiol. and Res., Porton Down, Salisbury, Wiltshire SP4 0JG UK
SOURCE: Quesnel, L. B. [Editor]; Gilbert, P. [Editor]; Handley, P. S. [Editor]. Society for Applied Bacteriology Symposium Series, (1993) No. 22, pp. 43S-51S. Society for Applied Bacteriology Symposium Series; Microbial cell envelopes: Interactions and biofilms.
Publisher: Blackwell Scientific Publications Osney Mead, Oxford OX2 0EL, England.
Meeting Info.: Meeting Manchester, England, UK July 1992
ISSN: 0300-9610.
DOCUMENT TYPE: Article
LANGUAGE: English

L7 ANSWER 23 OF 29 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 93:405036 SCISEARCH
THE GENUINE ARTICLE: LJ555
TITLE: ENVELOPE STRUCTURE AND THE DEVELOPMENT OF NEW **VACCINES**
AUTHOR: ROBINSON A (Reprint); MELLING J
CORPORATE SOURCE: PUBL HLTH LAB SERV, CTR APPL MICROBIOL & RES, DIV BIOL, SALISBURY SP4 0JG, WILTS, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND
SOURCE: JOURNAL OF APPLIED BACTERIOLOGY, (1993) Vol. 74, Supp. S, pp. S43-S51.
ISSN: 0021-8847.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; AGRI
LANGUAGE: ENGLISH
REFERENCE COUNT: 52

L7 ANSWER 24 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1992-058283 [08] WPIDS
TITLE: New **immunogenic** conjugate - comprises antigen bound to filamentous haemagglutinin of Bordetella pertussis, used as carrier for conjugate **vaccines**.
DERWENT CLASS: B04 D16
INVENTOR(S): COWELL, J L; DICK, W E; KIMURA, A
PATENT ASSIGNEE(S): (AMCY) AMERICAN CYANAMID CO
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 471177	A	19920219	(199208)*		
R: AT BE CH DE ES FR GB GR IT LI NL SE					
NO 9103130	A	19920214	(199216)		
AU 9181789	A	19920220	(199218)		
CA 2048917	A	19920214	(199218)		
FI 9103820	A	19920214	(199219)		
JP 04230634	A	19920819	(199241)		7
EP 471177	A3	19930224	(199348)		
AU 649700	B	19940602	(199427)		
EP 471177	B1	19951004	(199544)	EN	9
R: AT BE CH DE DK ES FR GB GR IT LI NL SE					
DE 69113564	E	19951109	(199550)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 471177	A	EP 1991-110919	19910702
FI 9103820	A	FI 1991-3820	19910812
JP 04230634	A	JP 1991-222392	19910808
EP 471177	A3	EP 1991-110919	19910702
AU 649700	B	AU 1991-81789	19910812
EP 471177	B1	EP 1991-110919	19910702
DE 69113564	E	DE 1991-613564	19910702
		EP 1991-110919	19910702

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 649700	B	Previous Publ.	AU 9181789
DE 69113564	E	Based on	EP 471177

PRIORITY APPLN. INFO: US 1990-565161 19900813
AN 1992-058283 [08] WPIDS
AB EP 471177 A UPAB: 19940120
An **immunogenic** conjugate comprises an antigen coupled to a filamentons haemogglutinin (**FHA**) of Bordetella pertussis or its immunologically active fragment, or to an immunologically cross-reactive mutant **FHA** of B pertussis or its portion.

Also claimed is an immuniogenic conjugate comprising polyribosylribitolphosphate (PRRP) coupled to a **FHA** of B pertussis or its immunologically active portion, or to an immunologically cross-reactive mutant of **FHA** of B pertussis or its portion. The anigen is a carbohydrate e.g. a bacterial capsular oligosaccharide or polysaccharide or their fragments, especially from H. influence, Streptococcus pneumoniae, Neiserria **meningitidis**, Klebsiella pneuamoniae, Pseudomonas aruginosa and Staphylococcus aureus, and is pref. PRRP.

USE/ADVANTAGE - The conjugates are used as a **vaccine**, and for treatment and prophylaxis of e.g. AIDs and post-exposive conditions. **FHA** acts as a carrier for antigens, e.g. bacteria, viruses and cellular microcomponents, as it is nontoxic, has a relatively high mol. weight and after conjugation with antigens retains both T- and B-cell epitopes. **FHA** may also help to protect against marginally or non-**immunogenic** antigens when they are conjugated to **FHA**. When the antigen is (PRRP) of Haemophilus influenzae type P the **vaccine** is against **meningitis**. Admin. is intradermal, transdermal (e.g. by slow release polymers) intransmuscular, intraperitoneal, intravenous, subcutaneous, oral and intranasal. @(8pp Dwg.No.0/0
ABEQ EP 471177 A UPAB: 19940120
An **immunogenic** conjugate comprises an antigen coupled to a filamentons haemogglutinin (**FHA**) of Bordetella pertussis or its immunologically active fragment, or to an immunologically cross-reactive mutant **FHA** of B pertussis or its portion.

Also claimed is an immuniogenic conjugate comprising polyribosylribitolphosphate (PRRP) coupled to a **FHA** of B pertussis or its immunologically active portion, or to an immunologically cross-reactive mutant of **FHA** of B pertussis or its portion. The anigen is a carbohydrate e.g. a bacterial capsular oligosaccharide or polysaccharide or their fragments, esp. from H. influence, Streptococcus pneumoniae, Neiserria **meningitidis**, Klebsiella pneuamoniae, Pseudomonas aruginosa and Staphylococcus aureus, and is pref. PRRP.

USE/ADVANTAGE - The conjugates are used as a **vaccine**, and for treatment and prophylaxis of e.g. AIDs and post-exposive conditions. **FHA** acts as a carrier for antigens, e.g. bacteria, viruses and cellular microcomponents, as it is nontoxic, has a relatively high mol. wt. and after conjugation with antigens retains both T- and B-cell epitopes. **FHA** may also help to protect against marginally or non-**immunogenic** antigens when they are conjugated to **FHA**. When the antigen is (PRRP) of Haemophilus influenzae type P the **vaccine** is

against **meningitis**. Admin. is intradermal, transdermal (e.g. by slow release polymers) intransmuscular, intraperitoneal, intravenous, subcutaneous, oral and intranasal. @(8pp Dwg.No.0/0

ABEQ EP 471177 B UPAB: 19951109

An **immunogenic** conjugate, comprising an antigen coupled to a **filamentous hemagglutinin** of Bordetella pertussis or an immunologically active portion thereof, or to an immunologically cross-reactive mutant **filamentous hemagglutinin** of Bordetella pertussis or portion thereof. Dwg.0/0

L7 ANSWER 25 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 91262882 EMBASE
DOCUMENT NUMBER: 1991262882
TITLE: Pediatric **immunizations** and adverse events.
AUTHOR: Lepow M.L.
CORPORATE SOURCE: Albany Medical College, Albany, New York 12208, United States
SOURCE: Current Opinion in Infectious Diseases, (1991) 4/4 (463-468).
ISSN: 0951-7375 CODEN: COIDE5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
007 Pediatrics and Pediatric Surgery
017 Public Health, Social Medicine and Epidemiology
047 Virology
LANGUAGE: English

L7 ANSWER 26 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 83099056 EMBASE
DOCUMENT NUMBER: 1983099056
TITLE: A malaria 'mitogen'-induced depressed immune response to **meningococcal** polysaccharide **vaccine** in BALB/c mice.
AUTHOR: Oyeyinka G.O.
CORPORATE SOURCE: Dep. Med., Immunol. Lab., Ahmadu Bello Univ. Hosp., Zaria, Nigeria
SOURCE: Immunology Letters, (1982) 5/6 (301-303).
CODEN: IMLED6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
004 Microbiology
008 Neurology and Neurosurgery
LANGUAGE: English

AB Uninfected female BALB/c mice were given a 4-daily intraperitoneal injection, of supernatants obtained from 24-h cultures of Plasmodium berghei infected and control mouse red blood cells, for 20 days. Each mouse was subsequently injected subcutaneously with 10 mg **meningococcal** (groups A and C combined) polysaccharide **vaccine**. Mean **meningococcal** haemagglutinating antibody titres obtained in mice pretreated with control supernatants were consistently higher, than those obtained in mice

pretreated with supernatants from malaria-infected red blood cell cultures, over a period of 14 days. The results suggest that a malaria 'mitogen' may be involved in the pathogenesis of the immunosuppression characteristic of this infection.

L7 ANSWER 27 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 81124980 EMBASE
DOCUMENT NUMBER: 1981124980
TITLE: Tuberculous **meningitis**: Immune reactions within the central nervous system.
AUTHOR: Kinnman J.; Fryden A.; Eriksson S.; et al.
CORPORATE SOURCE: Dept. Neurol. Infect. Dis., Univ. Hosp., Lonkoping S-581 85, Sweden
SOURCE: Scandinavian Journal of Immunology, (1981) 13/3 (289-296).
CODEN: SJIMAX
COUNTRY: Norway
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
015 Chest Diseases, Thoracic Surgery and Tuberculosis
004 Microbiology
008 Neurology and Neurosurgery
037 Drug Literature Index
LANGUAGE: English

AB Cerebrospinal fluid (CSF) lymphocytes from two patients with tuberculous **meningitis** proliferated stronger than the corresponding peripheral blood lymphocytes (PBL) when stimulated with tuberculin purified protein derivative (PPD) in the lymphocyte transformation test after 3 days of culture. This might indicate an accumulation of specifically primed lymphocytes within the central nervous system. CSF lymphocytes and PBL from nine of ten patients with acute aseptic **meningitis** investigated as controls showed no or low responses when stimulated with PPD, whereas the remaining patient displayed a significant proliferation of CSF lymphocytes, which was more pronounced than that of PBL. Stimulation with the mitogens phytohaemagglutinin, concanavalin A, and pokeweed mitogen gave lower proliferation of CSF lymphocytes compared with PBL in tuberculous and aseptic **meningitis**. Evaluation of the proliferative response of CSF lymphocytes compared with PBL on stimulation with PPD might be a useful complement in the diagnosis of tuberculous **meningitis**.

L7 ANSWER 28 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 82165096 EMBASE
DOCUMENT NUMBER: 1982165096
TITLE: Postsplenectomy infection.
AUTHOR: Francke E.L.; Neu H.C.
CORPORATE SOURCE: Dept. Int. Med., Abbott-Northwest. Hosp., Univ. Minnesota, Minneapolis, MN, United States
SOURCE: Surgical Clinics of North America, (1981) 61/1 (135-155).
CODEN: SCNAA7
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index

026 Immunology, Serology and Transplantation
009 Surgery
004 Microbiology
006 Internal Medicine

LANGUAGE: English

AB The period immediately after splenectomy entails a high risk of infection, which includes wound infections, pneumonia, urinary tract infections, and subphrenic abscesses. The risk of these infections increases with instrumentation as it does for other operations. The role of prophylactic use of antibiotics to prevent early postoperative infection has not been elucidated. There is no doubt that the risk of late infection due to pneumococci, H. influenzae, and possibly **meningococci**, staphylococci, and E. coli, is increased after splenectomy, even that which has been performed for trauma. Underlying disease and/or chemotherapy and radiation therapy contribute to the increased risk of infection. Studies that have shown no increase in infection have had too few patients or too short a follow-up period after splenectomy. Infection with parasites, Babesia sp., and malaria, also has an increased morbidity and mortality rate after splenectomy. An increased risk of disseminated herpes zoster has been suggested. The spleen is necessary for formation of opsonizing antibodies to encapsulated organisms and is the major site of phagocytosis in the absence of such antibodies. The high level of organisms present in overwhelming pneumococcal systemic infections, a frequent manifestation of pneumococcal infection after splenectomy, may be attainable because of a transient deficiency of the alternative pathway of complement. Tuftsin deficiency may play an as yet undefined role in infections after splenectomy, perhaps allowing an increase in late staphylococcal infection through diminished neutrophil phagocytosis. Cellular immunity may be deficient, contributing to the increased morbidity and mortality of Babesia sp. and malarial infections and to an increased risk of disseminated herpes zoster. Whenever possible, partial splenectomy or repair should be considered as an alternative to total splenectomy. All splenectomized patients should be **vaccinated** with pneumococcal **vaccine**.
Patients who will undergo staging splenectomy or removal of the spleen for other reasons should receive the pneumococcal **vaccine** before the procedure if at all possible. Use of the **meningococcal vaccine** should be considered. When a suitable H. influenzae B **vaccine** is available, it should be used. Those with low initial levels of antibodies to pneumococci or those with a high risk of exposure, those on chemotherapy for lymphoreticular or other malignant disorders, those under five years of age, and possibly all patients in the first two or three years after splenectomy, should receive prophylactic penicillin therapy (penicillin V or amoxicillin). Trimethoprim-sulfamethoxazole or erythromycin can be used in patients allergic to penicillin. Any 'flu-like' illness after splenectomy should prompt the taking of cultures and treatment with an anti-pneumococcal, anti-H. influenzae antibiotic, since early treatment may reduce morbidity and mortality pending culture results. The splenectomized patient should be warned of the risk of infection from encapsulated bacteria, particularly S. pneumoniae and H. influenzae.

L7 ANSWER 29 OF 29 EMBASE on STN

ACCESSION NUMBER: 77138879 EMBASE

DOCUMENT NUMBER: 1977138879
TITLE: 1975 Current results of the first 100 cytologically typed acute lymphoid leukemia submitted to BCG active immunotherapy.
AUTHOR: Mathe G.; De Vassal F.; Delgado M.; et al.
CORPORATE SOURCE: Inst. Cancerol. Immunogenet., Hop. Paul Brousse, Villejuif, France
SOURCE: Cancer Immunology Immunotherapy, (1976) 1/1-2 (77-86).
CODEN: CIIMDN
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
037 Drug Literature Index
LANGUAGE: English

AB The first 100 acute lymphoid (and undifferentiated) leukemias, (of which the smears at the first presentation of the disease were still available for typing), treated successively with remission induction chemotherapy, complementary cell reducing chemoradiotherapy and then active immunotherapy with irradiated pooled allogeneic leukemic cells and fresh Pasteur Institute BCG applied on scarifications, were reviewed, especially in connection with BCG application. Tolerance of BCG has been good. Its application had to be stopped due to a side effect (choroiditis) in only 1 patient. This toxic cost is negligible compared to that of so called maintenance chemotherapy. No subject of the first control trial started in 1963 has relapsed between 3 and 13 yr. In the overall group of the 100 patients studied, no relapse has been observed after 48 mth, which is quite different to the observations of frequent relapses after that time in patients submitted to maintenance chemotherapy. Moreover, second remissions are obtained in 94% of the patients who relapsed early under immunotherapy, and their life expectancy after a second remission is as high as it is after the first remission. The median of survival is longer than 5 yr. The action of active immunotherapy on the immune machinery was followed by several assays, of which the increase of null cells (which include K cells) may be the most interesting. Several prognostic factors were demonstrated among which are sex, the volume of the neoplasia, mesangial localizations, and the cytological types. Age has no prognostic value in immunotherapy patients, contrary to maintenance chemotherapy patients. Also the cytological types behave differently under immunotherapy and under maintenance chemotherapy. The disease free survival of more than 85% of the microlymphoblastic patients submitted to immunotherapy was not observed in J. Bernard's patients submitted to maintenance chemotherapy, which suggests that this high cure rate is due to active immunotherapy. Hence, these prognostic factors are probably factors of sensitivity to active immunotherapy. A statistical computerized study has shown that there is a link between the cytological types and other prognostic factors and that they all depend on the cytological type. Hence, the present protocol is adapted to this immunotherapy sensitivity factor. It comprises a nonrisk preimmunotherapy chemotherapy for the microlymphoblastic type, and a longer and more intensive chemotherapy for less immunotherapy sensitive types.

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 12:18:51 ON 08 OCT 2003)
L8 343 S "NASSIF X"?/AU
L9 233 S "TINSLEY C"?/AU

-Author (s)

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L10         295 S "KLEE S"?/AU
L11         680 S "ACHTMAN M"?/AU
L12         232 S "MERKER P"?/AU
L13           6 S L8 AND L9 AND L10 AND L11 AND L12
L14          65 S L8 AND (L9 OR L10 OR L11 OR L12)
L15           9 S L9 AND (L10 OR L11 OR L12)
L16          11 S L10 AND (L11 OR L12)
L17          11 S L11 AND L12
L18           3 S (L14 OR L8 OR L9 OR L10 OR L11 OR L12) AND L4
L19          18 S L13 OR L15 OR L16 OR L17 OR L18
L20           6 DUP REM L19 (12 DUPLICATES REMOVED)
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L20 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2001:50126 HCAPLUS
DOCUMENT NUMBER: 134:130251
TITLE: Neisseria **meningitidis** compounds and anti-infection applications thereof
INVENTOR(S): **Nassif, Xavier; Tinsley, Colin**
PATENT ASSIGNEE(S): Institut National De La Sante Et De La Recherche Medicale (Inserm), Fr.; Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften E.V.
SOURCE: Eur. Pat. Appl., 237 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1069133	A1	20010117	EP 1999-401764	19990713
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2001004150	A2	20010118	WO 2000-EP6943	20000705
WO 2001004150	A3	20011213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1194446	A2	20020410	EP 2000-956222	20000705
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: EP 1999-401764 A 19990713
WO 2000-EP6943 W 20000705

AB The invention provides novel Neisseria **meningitidis** (Nm) polypeptides and polynucleotides which cover the Nm genetic diversity, and which correspond to polypeptide of Nm outer membrane and/or periplasma, and to methods for producing such Nm compds. Also provided are anti-Nm infection, and particularly diagnostic, prophylactic and therapeutic uses thereof.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE

IN THE RE FORMAT

L20 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2000:213592 HCAPLUS
DOCUMENT NUMBER: 133:145715
TITLE: Molecular and biological analysis of eight genetic islands that distinguish Neisseria **meningitidis** from the closely related pathogen Neisseria gonorrhoeae
AUTHOR(S): **Klee, Silke R.**; **Nassif, Xavier**; Kusecek, Barica; **Merker, Petra**; Beretti, Jean-Luc; **Achtman, Mark**; **Tinsley, Colin R.**
CORPORATE SOURCE: Max-Planck Institut fur Molekulare Genetik, Berlin, 14195, Germany
SOURCE: Infection and Immunity (2000), 68(4), 2082-2095
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pathogenic species Neisseria **meningitidis** and Neisseria gonorrhoeae cause dramatically different diseases despite strong relatedness at the genetic and biochem. levels. N. **meningitidis** can cross the blood-brain barrier to cause **meningitis** and has a propensity for toxic septicemia unlike N. gonorrhoeae. Subtractive hybridization has been used to identify DNA sequences which might encode functions specific to bacteremia and invasion of the meninges because they are specific to N. **meningitidis** and absent from N. gonorrhoeae. This report shows that these sequences mark 8 genetic islands that range in size from 1.8 to 40 kb and whose chromosomal location is constant Five of these genetic islands were conserved within a representative set of strains and/or carried genes with homologies to known virulence factors in other species. These were deleted, and the mutants were tested for correlates of virulence in vitro and in vivo. This strategy identified one island, region 8, which is needed to induce bacteremia in an infant rat model of **meningococcal** infection. Region 8 encodes a putative siderophore receptor and a disulfide oxidoreductase. None of the deleted mutants was modified in its resistance to the bactericidal effect of serum. Neither were the mutant strains altered in their ability to interact with endothelial cells, suggesting that such interactions are not encoded by large genetic islands in N. **meningitidis**.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2000:250828 HCAPLUS
DOCUMENT NUMBER: 132:261300
TITLE: Complete DNA sequence of a serogroup A strain of Neisseria meningitidis Z2491
AUTHOR(S): Parkhill, J.; **Achtman, M.**; James, K. D.; Bentley, S. D.; Churcher, C.; **Klee, S. R.**; Morelli, G.; Basham, D.; Brown, D.; Chillingworth, T.; Davies, R. M.; Davis, P.; Devlin, K.; Feltwell, T.; Hamlin, N.; Holroyd, S.; Jagels, K.; Leather, S.; Moule, S.; Mungall,

K.; Quail, M. A.; Rajandream, M.-A.; Rutherford, K. M.; Simmonds, M.; Skelton, J.; Whitehead, S.; Spratt, B. G.; Barrell, B. G.
CORPORATE SOURCE: The Sanger Centre, The Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 ISA, UK
SOURCE: Nature (London) (2000), 404(6777), 502-506
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The complete genome sequence was determined for a serogroup A strain of Neisseria meningitidis, Z2491. The sequence is 2,184,406 bp in length, with an overall G+C content of 51.8%, and contains 2121 predicted coding sequences. The most notable feature of the genome is the presence of many hundreds of repetitive elements, ranging from short repeats, positioned either singly or in large multiple arrays, to insertion sequences and gene duplications of one kilobase or more. Many of these repeats appear to be involved in genome fluidity and antigenic variation in this important human pathogen.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1998:71228 HCAPLUS
DOCUMENT NUMBER: 128:164910
TITLE: Genes and gene products specific to pathogenicity of Neisseria meningitidis, methods for obtaining them and their biological applications
INVENTOR(S): Nassif, Xavier; **Tinsley, Colin**; **Achtman, Mark**; Ruelle, Jean-Louis; Vinals, Carla; **Merker, Petra**
PATENT ASSIGNEE(S): Institut National De La Sante Et De La Recherche Medicale (INSERM), Fr.; Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften E.V., Berlin; Smithkline Beecham; Nassif, Xavier; Tinsley, Colin; Achtman, Mark; Ruelle, Jean-Louis; Vinals, Carla; Merker, Petra
SOURCE: PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9802547	A2	19980122	WO 1997-FR1295	19970711
WO 9802547	A3	19980409		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

CM, GA, GN, ML, MR, NE, SN, TD, TG

FR 2751000	A1	19980116	FR 1996-8768	19960712
FR 2751000	B1	19981030		
AU 9736977	A1	19980209	AU 1997-36977	19970711
AU 730423	B2	20010308		
EP 951552	A2	19991027	EP 1997-933727	19970711
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001504684	T2	20010410	JP 1998-505685	19970711
US 2002164603	A1	20021107	US 2001-928457	20010814

PRIORITY APPLN. INFO.:

FR 1996-8768	A	19960712
WO 1997-FR1295	W	19970711
US 1999-214759	B1	19990422

AB DNA sequences that are found in Neisseria meningitidis that are unique to it, specific to pathogenesis, and not found in N. gonorrhoeae, N. lactamica or N. cinerea are cloned by representational difference anal. A number of genes associated with pathogenesis that are found in N. meningitidis and N.gonorrhoeae including the genes of biosynthesis of the polysaccharide capsule (frpA, frpC, porA), pilC, the genes for rotamase, IgA protease, pilin, transferring-binding proteins and opacity proteins and the sequence IS1106. The genes map in clusters in three regions of the chromosome. The gene products can be used as antigens in the raising of antibodies for diagnostic or therapeutic uses, e.g. specific immunoassays or vaccines. The roles of the genes in pathogenesis can be studied by targeted deletion.

L20 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER:	97197173 MEDLINE
DOCUMENT NUMBER:	97197173 PubMed ID: 9044262
TITLE:	Two-dimensional structure of the Opc invasin from Neisseria meningitidis.
AUTHOR:	**Merker P**; Tommassen J; Kusecek B; Virji M; Sesardic D; **Achtman M**
CORPORATE SOURCE:	Max-Planck Institut fur molekulare Genetik, Berlin, Germany.
SOURCE:	MOLECULAR MICROBIOLOGY, (1997 Jan) 23 (2) 281-93. Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY:	ENGLAND: United Kingdom
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
OTHER SOURCE:	GENBANK-M80195; GENBANK-X78221
ENTRY MONTH:	199705
ENTRY DATE:	Entered STN: 19970609 Last Updated on STN: 19970609 Entered Medline: 19970527

AB A two-dimensional structural model was devised for the Opc outer membrane protein invasin which contains 10 transmembrane strands and five surface-exposed loops. One continuous epitope recognized by three monoclonal antibodies was localized to the tip of loop 2 by synthetic peptides and site-directed mutagenesis while a second, discontinuous epitope recognized by a fourth antibody was localized to loops 4 and 5 by insertion mutagenesis. These monoclonal antibodies are bactericidal and inhibit adhesion and invasion. Most of the T-cell epitopes defined by Wiertz et al. (1996) were localized to the transmembrane strands. Oligonucleotides encoding a foreign epitope (nabla) from Semliki Forest virus were inserted into

BglII restriction sites created by site-directed mutagenesis. The nabla epitopes inserted in all five predicted loops were recognized on the cell surface of live Escherichia coli bacteria by a monoclonal antibody and are exposed while nabla epitopes in the N-terminus or three predicted turns were not. The results thus confirm important predictions of the model and define five permissive sites within surface-exposed loops which can be used to insert foreign epitopes.

L20 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:649672 HCAPLUS
DOCUMENT NUMBER: 117:249672
TITLE: Immunobiology of Neisseria porin proteins and mapping of epitopes with vaccine potential
AUTHOR(S): Heckels, J. E.; **Tinsley, C. R.**; Butt, N.; McGuinness, B.; Virji, M.; Lambden, P. R.; Clarke, I. N.
CORPORATE SOURCE: Med. Sch., Univ. Southampton, Southampton, SO9 4XY, UK
SOURCE: Neisseriae 1990, Proc. Int. Pathog. Neisseria Conf., 7th (1991), Meeting Date 1990, 235-40. Editor(s): **Achtman, Mark.** de Gruyter: Berlin, Germany.
CODEN: 58FNAF
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Gonococcal strains express a single porin protein PI. Immunol. studies of PI have revealed two major classes (PIA and PIB), and these can be further subdivided into a number of different serovars. Meningococci express 2 rather than 1 porin protein, class 1 and class 2/3 proteins, which are responsible for subtype and serotype specificity, resp. This study concerns the immunochem. anal. of such protective epitopes on gonococcal PIB and meningococcal class 1 protein.

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